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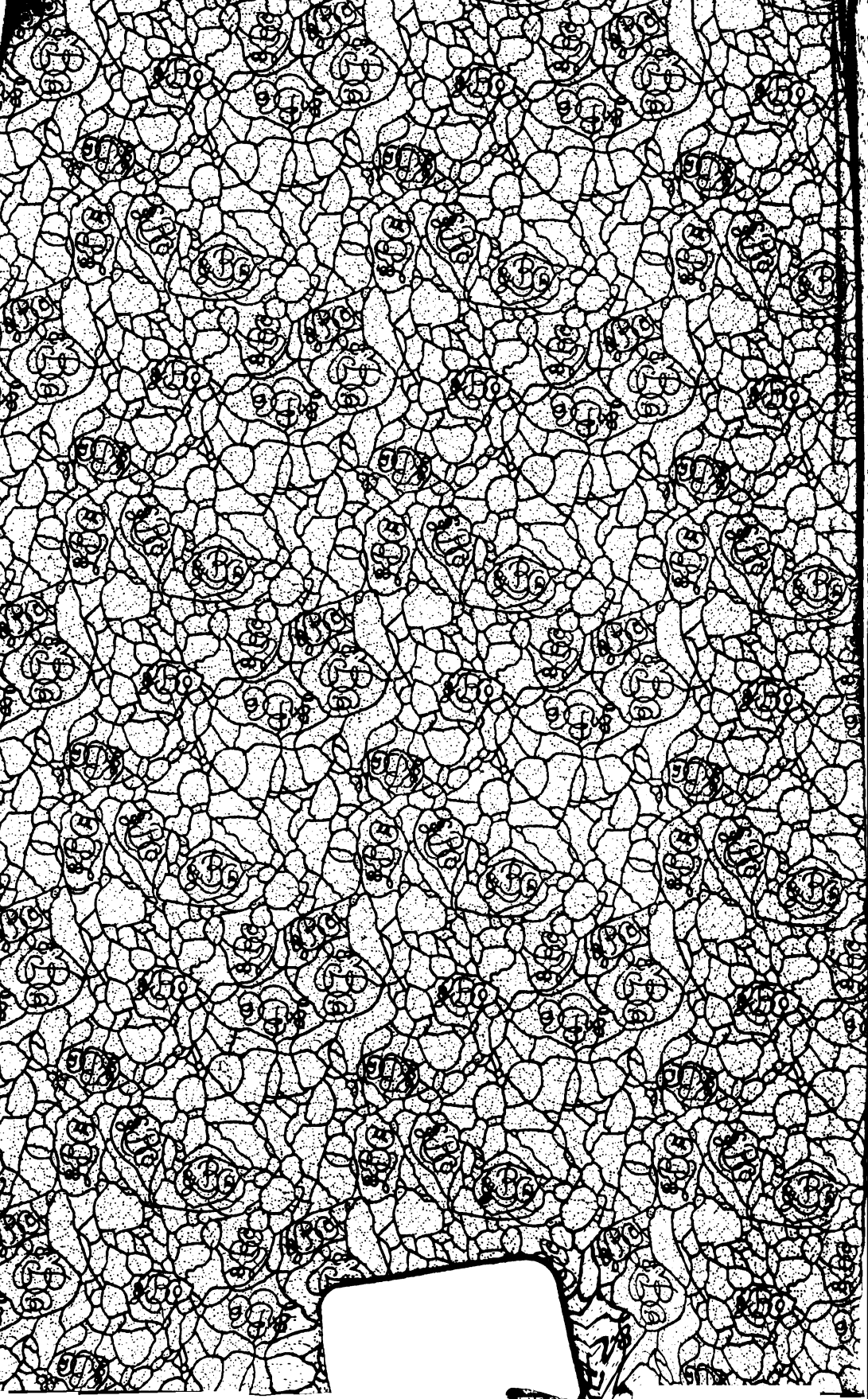
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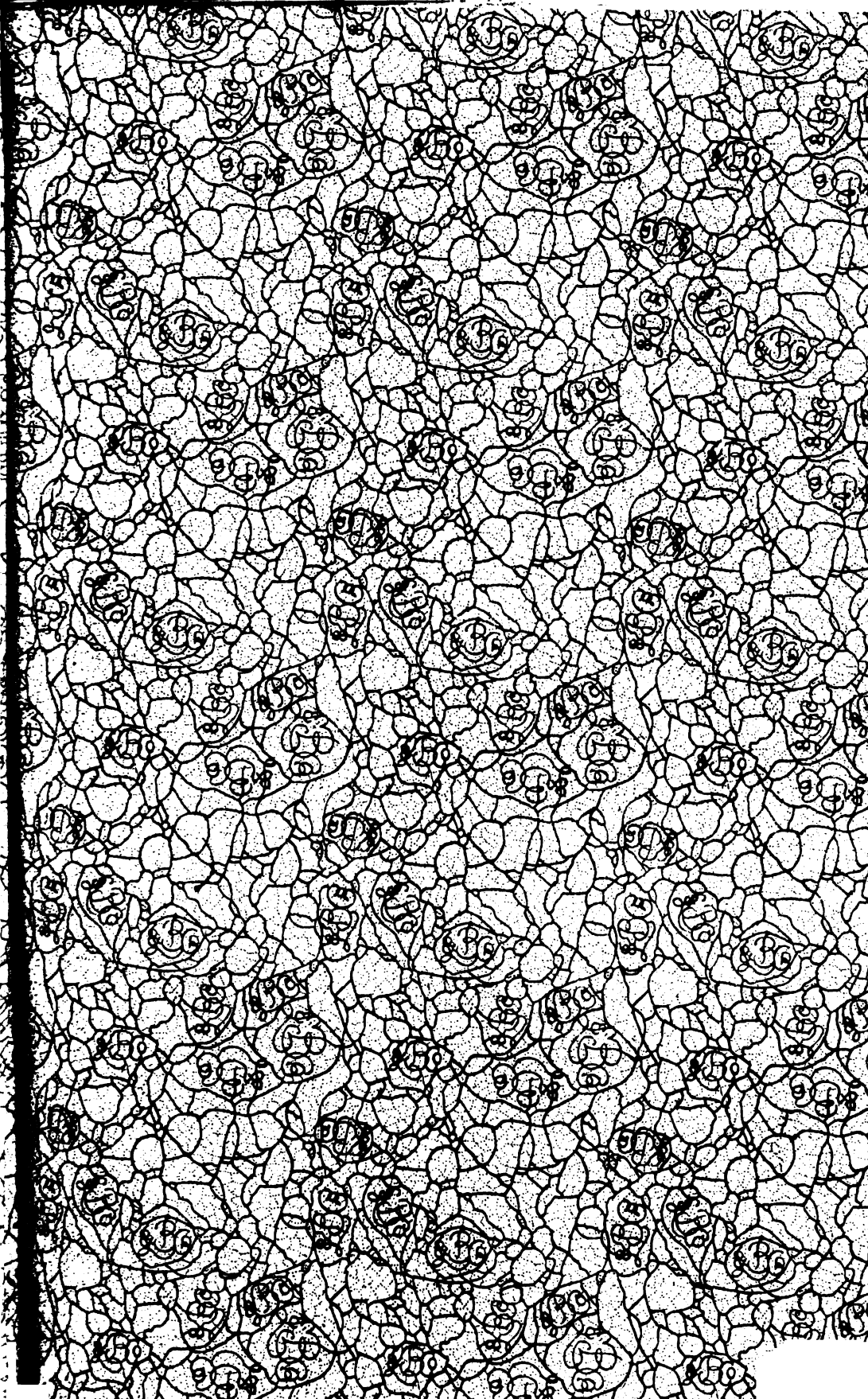
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PROGRESSIVE MEDICINE.

A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES,
AND IMPROVEMENTS

IN THE

MEDICAL AND SURGICAL SCIENCES.

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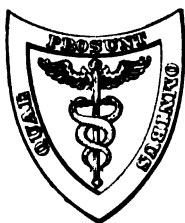
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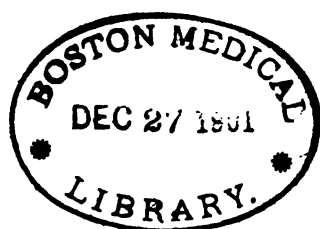
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DISEASES OF DIGESTIVE TRACT AND ALLIED ORGANS: LIVER, PANCREAS, AND PERITONEUM—GENITO-URINARY DISEASES—ANÆSTHETICS, FRACTURES, DISLOCATIONS, AMPUTATIONS, SURGERY OF THE EXTREMITIES, AND ORTHOPEDICS—DISEASES OF THE KIDNEYS—PHYSIOLOGY—HYGIENE—PRACTICAL THERAPEUTIC REFERENDUM.



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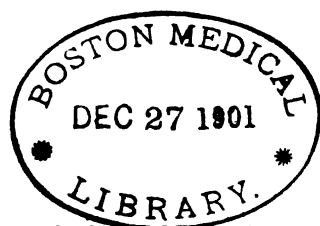
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PROGRESSIVE MEDICINE.

DECEMBER, 1901.

DISEASES OF THE DIGESTIVE TRACT AND ALLIED ORGANS, THE LIVER, PANCREAS, AND PERITONEUM.

BY MAX EINHORN, M.D.

THE ŒSOPHAGUS.

Diverticulum of the Lower Part of the Œsophagus. F. A. R. Jung¹ describes a case with a diverticulum at the lower end of the Œsophagus, and gives the following points of differential diagnosis between diverticulum and idiopathic dilatation of the Œsophagus :

1. With dilatation as well as with diverticula there occur painful cardiospasms as well as painless cases.

2. In both vomiting occurs from the Œsophagus, and occasionally from the stomach. Even in cases of typical cardiospasm eructation from the stomach may occur.

3. If food is vomited which has been eaten one or two days before while other food eaten in the meantime remains down the case seems to be one of diverticulum. No observations to the contrary have so far been made.

4. The swallowing sounds are abnormal in all cases of dilatation. In cases of diverticula the swallowing sounds are audible in 33 per cent., and can be used for diagnostic purposes. Westphalen's sound can also be heard in diverticulum with dilatation of the Œsophagus.

5. If after entering the Œsophagus it is easy to enter the stomach, a diverticulum probably exists; yet the passage of the tube may be difficult. "Only once out of ten experiments does one find the cardia and gain entrance into the stomach."

6. In making Rumpell's test, proof must be furnished that the tube is actually in the stomach. Inflation in this case is impossible, as feeling of the sound is not always practicable.

¹ American Journal of the Medical Sciences, April, 1900.

7. The proof positive of having entered the stomach is obtaining gastric juice through the inner tube.

8. Mercier's sound or Leube's diverticulum tube are necessary in order to find the entrance into the stomach. These tubes must be perforated for the diverticulum test, and by means of a thin inner tube gastric juice can be brought up.

9. After a diverticulum has been diagnosed its height can be ascertained (a) by Kelling's test (swallowing sounds) and (b) by filling the diverticulum with a colored solution and putting a narrow strip of white adhesive plaster longitudinally on the tube.

10. Neubauer's experiment for ascertaining the level of the liquid can also be used, according to Kelling, to determine the entrance into the diverticulum.

11. The entrance of the diverticulum can easily be overlooked by œsophagoscopy.

12. Gastrodiaphany did not show the diverticulum in Mintz's case, and gave no information about the kind of enlargement. In Reitenstein's case it was possible to make the diagnosis diverticulum by gastrodiaphany alone.

13. X-rays show an enlargement of the œsophagus only.

14. The statements of even the most experienced patient, that the tube is in the stomach, are often erroneous. The bending of the tube gives the patient and physician alike a sensation as though the tube had entered the stomach.

Idiopathic Dilatation of the Œsophagus. Ten new cases of dilatation of the œsophagus without any mechanical obstacle have been reported by me.¹

DIAGNOSIS. Idiopathic dilatation of the œsophagus will be diagnosed when dysphagia of long standing exists, the swallowing sound is found absent, no organic stricture encountered, and the œsophagus found partly filled with unaltered food.

The differential diagnosis must exclude malignant growths, a low-sitting diverticle of the œsophagus, and an antrum cardiae.

A malignant growth which has not led to a stricture is never accompanied by dilatation of the œsophagus; moreover, the swallowing sound will be found present. The general signs of malignant disease will also be discovered.

A low-sitting diverticulum occurs but rarely. Its existence may be excluded if the bougie or tube always enters the stomach without much difficulty. Rumpel has suggested the examination with two tubes, as mentioned above, in order to differentiate between diverticulum and

¹ American Journal of the Medical Sciences, September, 1900.

dilated œsophagus. It appears to me that Rumpel's method should be applied only in those cases in which the tube often fails to enter the stomach; otherwise we can be pretty sure that we have to deal with dilatation of the œsophagus, and not with a diverticulum.

An antrum cardiæ, which occasionally occurs, is but a very small sacculation, containing only at the utmost 50 c.cm. The latter will therefore be excluded if we find that the cavity above the stomach is able to hold 200 or more c.cm. Transillumination, œsophagoscopy, and X-ray examinations of the œsophagus have also been used for diagnostic purposes in this affection.

PROGNOSIS. The prognosis is good for life, but bad as regards complete recovery. All of my cases improved considerably and very quickly; the patients were all able to attend to their daily vocations and to enjoy almost perfect health, with the single exception that the dysphagia continued.

TREATMENT. The diet should consist of liquid, semiliquid, and solid foods rich in nutritious material. After each meal the patient must be instructed to perform exercises, consisting in compression of his chest after deep inspirations for a few minutes; this serves to force the food down from the œsophagus into the stomach.

Lavage of the (Esophagus. Every evening before retiring the œsophagus should be emptied and washed out by means of a tube.

The application of the faradic and also of the galvanic current within the œsophagus has been recommended by Rosenheim and others. I had the opportunity to make use of the faradic as well as of the galvanic current on one of my patients, but without the slightest benefit whatever. Feeding through a stomach-tube has been tried without permanent relief.

A sufficient diet, the exercises of forcing the food down, and lavage of the œsophagus are the essential points. Bromide, iron, and arsenic may also be of benefit.

THE STOMACH.

Iodipin as a Means of Determining the Motor Function of the Stomach. As is well known, iodipin forms a combination of iodine and fat which is not decomposed in the stomach. S. Heichelheim¹ made use of iodipin for testing the motor function of the stomach in a similar manner to that of salol. He administers 1.6 gramme of iodipin in gelatinous capsules at breakfast. The saliva is then examined every fifteen minutes for the presence of iodine (by means of

¹ Zeitschrift f. klinische Medicin, 1900, p. 321.

starch-paper and fuming nitric acid). He found that in most instances the reaction appeared before the end of an hour except in cases of pyloric obstruction, when it was greatly retarded.

The Action of Rennin. T. H. Coriat,¹ in an extensive study undertaken by him with regard to the action of rennin, sums up the function of this ferment as follows :

1. It splits up the casein into more easily digestible proteids.
2. These resulting proteids, therefore, are converted into albumose-peptone more easily and quickly than is the casein as it exists ordinarily in milk.
3. When rennin is present there is produced, in every case, with the proteolytic enzymes, more albumose-peptone.
4. Rennin assists the action of pepsin and pancreatin.

The conclusions Coriat arrives at relating to the action of rennin in the digestion and coagulation of milk are as follows :

ACTION OF RENNIN IN DIGESTION. 1. The casein of milk can be digested by both pepsin and pancreatin without being first coagulated by rennin.

2. When, however, rennin is present, in order to precipitate the casein the amount of digested proteid or albumose-peptone produced by the proteolytic enzymes above mentioned is greater in every case.

3. The presence of rennin is necessary to secure a more rapid and energetic casein digestion.

4. This increased peptone production, due to the presence of rennin, takes place in both acid (pepsin) and alkaline (pancreatic) media.

ACTION OF RENNIN ON COAGULATION. 1. Combined HCl, when equal in bulk to one-tenth or less of the milk used, does not coagulate milk, even after prolonged action.

2. Combined HCl, when it exceeds one-tenth of the bulk of milk used, coagulates with rapidity, although not as rapidly as when HCl is free.

3. Free HCl alone coagulates milk.

4. Rennin coagulates milk without HCl being present, but when it is present in a combined form equal to one-tenth or less of the bulk of milk used, coagulation takes place in a much shorter period.

5. The presence of acid-albumin hastens coagulation by the enzymes.

6. Coagulation time decreases steadily as greater amounts of absolute rennin are present.

7. Vegetable enzymes coagulate milk in a way which compares very favorably with rennin.

8. Coagulation with vegetable enzymes takes place under the same conditions of temperature, acidity, and amount as rennin.

¹ Philadelphia Medical Journal, July 14, 1900.

9. Enzymes exist in the plant kingdom which have an action analogous to that of rennin.

The Bacteria of the Stomach. J. H. Kellogg¹ has undertaken numerous investigations with regard to the number of bacteria in the stomach in different diseases and the influence of different foods on them. He found that fresh fruits and fruit-juices diminished the number of bacteria. In Kellogg's opinion the therapeutic value of fruit is beyond estimation. Fruit is a natural intestinal antiseptic. A fruit diet for a few days may always be relied upon to relieve an attack of so-called "biliousness." The adoption of a fruit diet when migraine or sick headache is impending will generally abort the attack if it does not altogether prevent it.

Kellogg arrives at the following conclusions :

1. A healthy stomach does not require the aid of germs in the digestion of foods.

2. Sterile food is digested in the healthy stomach without the development of bacteria or other micro-organisms.

3. Neither free hydrochloric acid nor combined chlorine, even when present in excess, are certain means of sterilizing the gastric contents.

4. The gastric contents may be found sterile after a sterile test-meal in cases in which free hydrochloric acid is entirely absent and the proportion of combined chlorine small.

5. Fruits, especially fresh fruits, and fruit-juices, are capable of completely sterilizing the stomach when used in sufficient quantity.

Bread and Bacteria. A. W. Perry,² in a study on the digestion of bread, found that any ordinary well-baked bread does not contain pathogenic germs.

"Although it is true that the heat of baking bread is insufficient to kill the spores of most bacteria, and also the pathogenic bacteria themselves, yet it does kill those bacteria which have been thought to have either a causal or aggravating action on stomach disorders, namely, the bacteria of alcoholic, lactic, acetic, and butyric fermentations, and also the sarcinæ. In Walsh and Waldo's experiments they found none of these bacteria. The eleven varieties they found were : hay bacilli, four kinds ; sarcina, two kinds ; four bacilli, named A, B, C, D ; bacillus figurans ; one staphylococcus ; micrococcus, A. The loaves in which these were found were large four-pound loaves, to the centre of which the heat reaches very imperfectly.

"None of these was pathogenic, and the only one which had any connection with gastric diseases was sarcina. Whether this relation is causal or sequential is doubtful. The bacteria which are supposed

¹ Virginia Medical Semi-Monthly, December 21, 1900.

² Pacific Medical Journal, September, 1900.

either to cause or to aggravate existing gastric diseases, viz., the bacteria of alcoholic, acetic, lactic, and butyric fermentation, were not found at all. Indeed, it is not likely they would be, for they are killed at the low temperature found in the centre of loaves of bread (163° F.) during the baking. George Newman says that a temperature of 158° F. kills the sour fermentation bacteria."

Perry's experiments give the following results. The samples of bread were taken from the interior of the loaves or rolls, placed in sterile water, and kept at 100° F. for three days in sterilized test-tubes.

Army crackers	Remained sterile.
French bread (one-pound loaves)	" "
Soft milk bread (one-pound loaves)	" "
Bakers' toast	" "
Hard rolls (three ounces)	" "

This is to be expected, as a heat of 160° F. is enough to kill the sour fermentation bacteria.

Under these findings, according to Perry, there is no reason for ascribing gastric disorders (fermentations) to the presence of living bacteria in bread, for the heat of baking loaves of less than two-pound weight is enough (203° F.) to kill all gastric fermentation bacteria which might have been in the materials used. Those found in the London examinations of Walsh were other innocent species, and these were found only in four-pound loaves. Dryness of bread with porosity, on which depends the amount of saliva which is absorbed in chewing, are the main factors in determining the digestibility of bread. If bread which is dry and porous is soaked in liquids before eating, or in the mouth while eating, its character of easy digestibility is taken away.

The Hydrochloric Acid Therapy. John C. Hemmeter¹ makes a strong plea for the administration of hydrochloric acid in digestive disorders accompanied by a deficient gastric secretion.

The purposes for which HCl is given in the absence or diminution of the normal secretion are: (1) To supplement gastric proteolysis; (2) to act as an antiseptic; (3) to act as a tonic and stomachic. The HCl is, according to Hemmeter, advantageous not for digestive purposes (for even with a large excess of HCl it is not the rule for all the proteid matter to be digested in the stomach), but for destroying the exuberance of micro-organisms swallowed with the food and for bringing about a proper reaction for the best digestive secretion of the pancreas.

On clinical as well as reliable experimental grounds Hemmeter feels justified in recommending hydrochloric acid, believing in its efficacy in supplementing the digestive work of the stomach in bringing about the normal conditions for duodenal digestion. Whenever it is indicated,

¹ American Medicine, April 20, 1901.

he usually gives 20 drops of the diluted HCl (U. S. P.) in 2 ounces of water every fifteen to twenty minutes, beginning fifteen minutes *before* the meal; then 20 drops are taken during the eating, and 20 drops half an hour after the meal. The medicine should always be taken through a glass tube, and the mouth rinsed with a weak solution of sodium carbonate afterward.

The cases frequently noted in patients without any gastric secretion whatever who succeed in maintaining their nitrogen equilibrium, and the experiment on the dog, the weight of which was kept up, although the largest portion of the stomach was removed, and Brigham's and Schlatter's total extirpations of the stomach, constitute but a weak argument against the therapy of HCl; for, although such patients and animals manage to get along fairly well for a time, it is only under the most careful and scientific supervision that their health is maintained. "Permanent and perfect health, with total absence of gastric secretion," Hemmeter says, "is rarely observed, except in those who are able to rest much and have their food prepared with great care."

I must say that I have observed quite a number of patients with achylia gastrica who did not require a careful diet, and who attended their daily vocations without any discomfort and without the need of partaking of any medicine whatever. The HCl therapy is quite old. Formerly its administration was overdone. It is only of late years that more definite indications for its use can be given. While I am of the opinion that HCl may be administered for some time (several weeks), in conditions accompanied by a deficient secretion of gastric juice, I do not think that it should be kept up permanently; nor do I think it is essential in the treatment of achylia gastrica.

Sedatives in Gastric Affections. F. Riegel¹ has studied the action of morphine and atropine on gastric secretion. According to his investigations, morphine increases the gastric secretion, while atropine lessens it. It appears, therefore, rational to administer atropine in painful gastric affections, accompanied by hyperchlorhydria, and to rather avoid the use of morphine in these cases.

Idiopathic Phlegmonous Gastritis. F. P. Kinnicutt² reports a case of phlegmonous or suppurative gastritis, in a man aged forty-one years. Kinnicutt describes the case as follows: Five days before admission to the hospital, after drinking to excess and after a hearty meal, he suddenly began to vomit. The vomited matter consisted at first of the food in the stomach, and later of a brownish fluid. Vomiting occurred frequently during the four subsequent days, irrespective of the ingestion of food, which was only fluid in character. There was never any blood

¹ Zeitschrift f. praktische Aerzte, 1900, No. 17.

² Philadelphia Medical Journal, November 17, 1900.

in the vomited matter. There was moderate diarrhoea for the first three days, and then no further movement of the bowels previous to admission. Blood was not present in the stools. With the onset of the vomiting he suffered from pain located in the epigastrium and in the lower abdomen. The pain was acute and more or less constant for the first three days. For two days previous to admission he was comparatively free from suffering. With the occurrence of the first symptoms of his illness there was a feeling of chilliness, but no distinct chill.

Examination on Admission. The patient was a large, muscular man, well nourished and not anæmic in appearance. The tongue was very dry and moderately coated. The respirations were shallow, 48 to the minute. The pulse was 108, full, and a little tense. Temperature (rectal), 101° F. The patient was very restless, anxious, and obviously very ill. Heart: The apex was in the fifth space, in the mid-clavicular line. The left limit of cardiac dulness in the fifth space corresponded with the apex impulse. No murmurs are appreciable. Lungs: Negative, beyond slight dulness at both bases and moderate subcrepitation over these areas. Liver: Percussed from the sixth rib to the costal arch, in the mid-clavicular line; edge not palpable. Spleen: Area of dulness not increased, edge not palpable. Abdomen: Was moderately distended, with considerable rigidity of the abdominal walls, most marked in the upper half. There was moderate sensitiveness on deep palpation and slight on gentle palpation, and this sign was not obtained uniformly over the abdomen, but at several points, being most marked over the epigastrium and right hypochondrium. It has been noted that the liver dulness is not obliterated, but fully reaches the costal arch, in the mid-clavicular line. Over the liver region, just above the costal arch, and also over the left hypochondrium, in the anterior axillary line, scanty crepitation was heard, and was believed to indicate an involvement of the peritoneum. Signs of free fluid in the peritoneal cavity are not obtained. Abdominal respiratory movement was present, but diminished. The urine was free from albumin and sugar; specific gravity, 1025. It contained a few hyaline and granular casts.

Lavage was immediately given, and a yellowish-brown fluid, without odor, considerably larger in amount than that introduced, was returned by siphonage. A general peritonitis was believed to exist; the causative lesion was judged to be either an acute pancreatitis or a perforating ulcer of the duodenum.

The advisability of an operation was considered; the patient's condition, however, rapidly growing worse, did not permit it. Death occurred sixteen hours after admission.

At the autopsy general peritonitis and diffuse suppurative gastritis were found. The principal seat of the lesion was the submucosa. This

layer was enormously thickened, measuring in certain places three-fourths of an inch even in the hardened section. It had evidently been the main seat of the bacterial infection. Its fibres were widely separated by quantities of fibrin, leucocytes, lymphocytes, and complete *strata* of bacteria. The violence of the inflammation had caused extensive areas of partial or complete necrosis; in these only the faintest outlines of cells and fibrils were distinguishable. The lymphatics were here and there gorged with microbes. Between the submucosa and the mucosa proper the necrotic spaces were less numerous, but vast numbers of lymphocytes (many more than those normally present) were found. The *muscularis mucosæ* was generally in place, and unexpectedly enough seemed to have participated in the pathological process less than any other layer of the entire stomach.

The bacteriological examination of the stomach, as described by Kinicutt, showed the practically universal presence of a streptococcus. It was most abundant in the connective tissue of the submucosa and muscularis. Some of the individual chains were quite long, being made up of eight and ten members, but most of them are shorter. Contrary to the classic descriptions, few or no cocci were to be found inside the leucocytes. The *strata* mentioned above were made up almost entirely of these chain cocci. The lymphatics contained not so many cocci as bacilli. The latter were long, with deeply stained ends (spores?). They were possibly of post-mortem origin, inasmuch as they were abundant in the superficial vessels. No cultures were made from the stomach, but films made from the exudate on the cut surface show that the streptococcus was the prevailing pathogenic organism.

Ulcer of the Stomach. W. Körte¹ publishes his experiences on the surgical treatment of ulcer of the stomach and its sequelæ, embodying thirty-eight operations. He is of the opinion that the surgical treatment of ulcer of the stomach and its complications—particularly stenosis of the pylorus and dilatation of the stomach—shows very good results in cases in which internal medicine fails. It therefore deserves wider recognition and application in these affections.

TREATMENT OF GASTRIC ULCER. Shattuck² discusses the medical treatment of peptic ulcer as follows: The gastric ulcer is subject to two adverse influences—the irritating acid secretion and the unrest due to the periodical changes in the size of the organ and to the peristalsis. The duodenal ulcer is subject only to the former. In spite of these adverse influences we know that healing may take place, but it would seem entirely reasonable to suppose that healing may be promoted by rest just as it is in every ulcer of the skin or mucous membrane which

¹ Deutsche med. Wochenschrift, March 21, 1901.

² Journal of the American Medical Association, April 13, 1901.

is accessible to vision. We have no means of knowing, in any given case, how large or deep an ulcer may be, or whether it is single or multiple. We know that surface ulcers of any depth or size do not heal in two or three days, and if the principle of absolute rest is worth being enforced at all in peptic ulcer it is worth strict enforcement; hence Shattuck adopted the arbitrary period of two weeks as a reasonable time to allow for the healing process and a fair average limit of toleration of exclusive rectal feeding. This period has been prolonged in two cases to five weeks, and has been shortened in others to meet the seeming demands of the special case. In a few cases rectal feeding has clearly provoked stomach unrest and vomiting. In some others the period of stomach abstinence has been shortened on account of the refusal of the bowel to retain or absorb in spite of various coaxings. In most cases all discomfort ceases as soon as the stomach ceases to work, and there is usually no great sense of hunger. If discomfort persists or hunger is importunate he gives small doses ($\frac{1}{32}$ to $\frac{1}{16}$ grain) of morphine once or more during the day.

Shattuck ordinarily gives a large cleansing enema daily and nutrient enemata every six hours. Formerly he rarely gave more than six ounces of milk or milk and egg—in either case with a pinch of salt—at a time. Lately he has found that in some cases as much as a pint of nourishment can be introduced and absorbed every six hours. For thirst small quantities of water by the mouth may be allowed; in other cases water may be introduced into the rectum or under the skin.

GASTRIC ULCER: ITS SURGICAL TREATMENT. In a lecture on gastric ulcer and its treatment Mayo Robson¹ asserts that in his private work he had a mortality of 5 per cent. from operations on the stomach. According to Robson, the surgical treatment of intractable or relapsing gastric ulcer is in the greater number of cases the only satisfactory method, and operation should be resorted to at a much earlier period than has hitherto been the custom, and always before patients are so far reduced by pain and starvation or the supervention of serious complications that their weakened condition renders any operation a serious matter.

The fact is that ulcer of the stomach is a much more serious matter than the profession generally recognizes, for, according to various authorities, it has an all-round rate of mortality, when medically treated, of from 20 to 50 per cent.; if, therefore, surgery can by operation save 95 per cent., or even a greater percentage, of the more serious cases, a real advance will have been made, for it must be borne in mind that ulcer of the stomach is a very common disease.

¹ British Medical Journal, February 2, 1901.

Gastro-enterostomy, of all operations, is the one to rely on in the treatment of gastric ulcer, and Robson prefers the posterior operation, which he performs after a method of his own, the junction of the stomach and first part of the jejunum being effected by two continuous sutures around a decalcified bone bobbin. The whole operation can be easily completed in half an hour or in twenty minutes. Robson's last twenty cases have all recovered without pain, vomiting, or any drawback.

Excision of the ulcer is as a rule unnecessary, but not always to be avoided.

Pyloroplasty, if the pylorus be stenosed, free from extensive adhesions, easily drawn forward, and not actively ulcerating, is a simple and short operation, and in several cases of gastric ulcer Robson has found it to answer well; but it must not be performed in the case of active ulceration of the pylorus itself unless the ulcer be at the same time excised, otherwise contraction will occur and further operative treatment will be demanded. Robson has had experience of this in one case where the patient put on weight after pyloroplasty and appeared to have completely recovered, but a year later stenosis recurred, and he had to perform gastro-enterostomy, which effectually cured her.

Pylorectomy is an unnecessarily severe operation for simple ulceration, and though he has performed it on three occasions, and the patients have recovered, he cannot see that it presents any advantage over gastro-enterostomy:

Pylorodiosis. Loreta's or Hahn's operation, which consists in stretching the pyloric sphincter, will be given up. Robson has seen two relapses after the operation, and he will not do it again, for it is more dangerous, as proved by statistics, and less satisfactory than gastro-enterostomy.

Erosions of the Stomach. E. Quintard¹ describes three cases of erosions of the stomach. The cases reported by Quintard resemble in their principal points those described by Einhorn; that is to say, in these cases there were the loss of flesh, the pain after eating not very intense, the exhaustion on exertion, the pinched and more or less haggard look at times, and finally that which rendered the diagnosis positive—namely, the repeated findings in the wash-water of little pieces of gastric mucosa. So far as treatment is concerned it would seem that excellent results are to be had with the solution of nitrate of silver of the strength of 2:1000 or stronger, sprayed by means of an Einhorn atomizer, this being done every other day. In the cases reported it can be seen that after two or three applications of the nitrate of silver

¹ Medical Record, September 15, 1900.

solution the fragments of mucosa, as a rule, ceased to appear in the wash-water, and in conjunction with this the subjective symptoms and the general condition of the patient improved. In a recent conversation on this subject the writer told Dr. Quintard that of late he has been using with seemingly good results¹ five grains of the extract of suprarenal gland, powdering the stomach with this amount while the latter organ was in the fasting condition.

The conclusions of Quintard, similar to those of the writer and Pariser, are as follows :

1. That from time to time we see patients in whose stomach-washings are repeatedly found small fragments of the gastric mucous membrane ; on an average one to four of such pieces are found in a washing, their size varying from 2 to 7 mm. long and about 2 to 3 mm. wide ; that the repeated findings of such pieces of mucosa in the wash-water show that we are dealing with a case of erosion.

2. That such erosions occur under varying pathological conditions, and that as a consequence the functional signs vary accordingly.

3. That the exact etiology and pathology of such erosions are at present not definitely known ; that in the great majority of cases, at least where such tiny fragments of mucous membrane are found in the wash-water, the patient gives a definite and peculiar clinical history distinct from that of round ulcer or from the exulceratio simplex described by Dieulafoy.

4. That as a consequence these cases should be regarded as a distinct class clinically and treated as such.

Volvulus of the Stomach. Wiesinger¹ describes a case of volvulus of the stomach, with occlusion of the cardiac and pyloric orifices and acute fat-necrosis. The patient, aged forty-one years, became sick quite suddenly after an ordinary meal, with symptoms of acute ileus. Soon there were vomiting, constipation, pains, and a bloated condition of the abdomen. The pains were especially intense in the left hypochondriac region. At the same place a swelling was noticeable, which slowly but gradually increased within the next few days. The symptoms steadily growing worse, the patient was subjected to a laparotomy. The peritoneal cavity was found filled with a sanguinolent fluid, the peritoneum showed all signs of beginning inflammation, and the omentum revealed numerous patches of fat-necrosis. The tumor was discovered to be the stomach turned upsidedown, and containing four quarts of liquid. In this peculiar position the stomach was kept by newly formed adhesions. After emptying this organ and loosening the adhesions, the stomach returned to its usual position. The patient made a rapid recovery.

¹ Deutsche med. Wochenschrift, February 7, 1901.

Gastro-intestinal Hemorrhage Due to a Degenerated Heart. C.

Phelps¹ reports a case of a patient who died from gastro-intestinal hemorrhages a few days after an operation for hernia. At the autopsy nothing was found in the digestive tract to account for the hemorrhage. The heart, however, showed fatty degeneration, principally in the right ventricle. Slight cirrhosis of the liver was also found. Phelps thus explains the fatal hemorrhage :

The extent to which the cirrhotic disease in the liver had advanced was obviously insufficient to account for the fatal gastro-intestinal hemorrhage ; but the condition of the heart seems to afford adequate explanation. The weakened heart, so long as no special stress was put upon it, continued to perform its function, but failed to respond to the additional strain involved in the administration of anæsthetics ; and, as often happens with degenerated hearts, was afterward unable to recover itself, even with the aid of constant and thorough stimulation and of equally strenuous effort directed toward the dilatation of the superficial capillaries. The special seat of degeneration in the right ventricle, and the entire dependence of symptoms upon this seat of disease, may be regarded as peculiar. The primary failure of the pulmonary circulation was evident in the extreme and persistent cyanosis of the patient during the whole period of anæsthesia. With the discontinuance of anæsthetics the blood passed more freely through the lungs, and cyanosis for a time disappeared ; but the ventricular contraction was still inadequate, and with the supervention of vomiting on the third day became still more incapable of transmitting blood through the lungs. Blood gradually accumulated in the right side of the heart, and secondarily in the inferior vena cava and portal system, till the overdistended gastro-intestinal vessels finally gave way. The resiliency of the lungs forced the last of the blood received through the pulmonary arteries into the left ventricle, which, less degenerate than the right, in turn forced it into the general circulation, and the left ventricle, like the lungs, was left empty and contracted. The final drainage of the pulmonary vessels of the lung was doubtless aided by the suction force exerted by an already approximately empty left ventricle.

The copious hemorrhage emptied to a large extent the portal veins, the inferior cava, and the right ventricle.

The Early Diagnosis of Gastric Cancer. G. W. McCaskey² points out the means at our disposal for establishing the diagnosis of gastric cancer. It is very difficult to formulate specific statements as to what would constitute a proper basis of diagnosis, because the same factors

¹ New York Medical Journal, February 9, 1901.

² Toledo Medical and Surgical Reporter, January, 1901.

will have a different value in different cases, and must therefore be carefully weighed in relation to the case under examination. Progressive increase of isochromia, with malnutrition; progressive diminution of free HCl, and of peptic digestion, with perhaps the addition of pain, the presence of lactic acid and the Oppler-Boas bacillus, with atypical mitosis, appear to be the most reliable data at present available. In the existing state of our knowledge it must be conceded that the early diagnosis of gastric cancer is one of the most difficult problems which confronts the clinician, and yet a thorough and practical study of all the data which have been indicated, applied to the circumstances and personality of the individual case, will enable us to often reach a diagnosis sufficiently early to give the patient an opportunity of receiving the benefits of a radical operation. This can be done with all the more boldness, inasmuch as exploratory laparotomies are now made with so small an element of danger that they are not entitled to very much weight in summing up the hazards of the situation as compared with the utter hopelessness of gastric cancer which has passed the operable stage. McCaskey, in discussing the surgical aspects of the question, says that its feasibility and utility have been absolutely demonstrated, and that the future of these cases rests largely upon the alertness, conscientiousness, and skill of the diagnostician and the boldness of the surgeon in meeting the exigencies of the case. There seems to be no doubt whatever that cancer is primarily a local disease, and if it can be attacked sufficiently early, and extirpated with a free, fearless, and relentless hand, the prospect of a radical cure may safely be said to be encouraging.

Bettman¹ entertains similar views as McCaskey, and also favors an exploratory laparotomy in doubtful cases.

DIGESTION LEUCOCYTOSIS IN CANCER OF THE STOMACH. Osler and McCrae² arrive at the conclusion that no reliance can be placed on digestion leucocytosis as an aid to the diagnosis of gastric cancer. The same opinion is represented by C. Douglas.³

The method employed by Douglas for ascertaining the presence or absence of digestion leucocytosis was as follows: In each case the blood was carefully examined and the leucocyte count determined in the fasting condition, generally about 11.45 A.M., or shortly before the hour of the hospital dinner. At noon a meal was given sufficiently rich in proteids to occasion a distinct leucocytosis in a healthy person. This meal usually consisted of ten ounces of milk beaten up with one or

¹ Cincinnati Lancet Clinic, November 24, 1900.

² Cancer of the Stomach, 1900, p. 119.

³ British Medical Journal, March 16, 1901.

two raw eggs, according to the state of the patient's stomach. The leucocyte count was then made again three hours later.

It would appear from the results obtained that digestion leucocytosis is a broken reed on which to lean in the diagnosis of cancer of the stomach, since only a trifle over 54 per cent. of the cases gave a positive reaction in regard to it.

Pernicious Anæmia and Malignant Disease of the Stomach. A. Abrams,¹ in a paper, "Progressive Pernicious Anæmia and Malignant Disease of the Stomach," arrives at the following conclusions:

1. Arsenic is a true specific in pernicious anæmia, and is as certain in its immediate results as is mercury in syphilis, quinine in malaria, or iron in chlorosis. The specificity of arsenic is so great that in no case of grave anæmia are we justified in excluding the progressive pernicious variety, even though the blood examination is negative, without a heroic trial of arsenic. Like the other specifics, it produces relative cures, and cannot be regarded as a prophylactic, owing to the frequent relapses which occur. It may be given as Fowler's solution, beginning with 3-minim doses, well diluted after each meal, and increased by 1 or 2 minims daily, according to the urgency of the case, until 25 or 30 minims are taken three times a day. A safer rule is to push it to the point of toleration and maintain it at this point until the blood examination shows the result desired. The appearance of its physiological effects (œdema and itching of the eyelids, gastro-intestinal irritation, etc.) is a signal for its temporary discontinuance. When arsenic cannot be given by the stomach it may be administered subcutaneously or even by the rectum.

2. In association with arsenic assimilable food and rest are indispensable adjuvants.

3. The use of intestinal antiseptics in this as well as in other diseases is a mere therapeutic refinement not sanctioned by bacteriological reasons, and they ought, therefore, not to be employed as a routine measure. In the Italian literature one finds some authentic evidence of the good effects from thymol, its administration being suggested by the theory that pernicious anæmia is caused by intestinal absorption of products which are destructive to the red blood-corpuscles.

4. Iron is not only useless, but is apt to create digestive disturbances.

5. Bone-marrow is said to be curative, but in my experience it induces nausea and aggravates existing gastro-intestinal troubles.

6. Gastric disturbances suggest stomach lavage. The character of the food digested must be determined by the results of a chemical analysis of the stomach contents.

¹ Medical Record, April 28, 1900.

7. To counteract the great reduction in the quantity of blood (oligæmia) weak saline solutions may be given by the colon (enteroclysis) or preferably in the subcutaneous tissue (hypodermoclysis).

8. Relapses are best prevented by minute attention to dietetic and hygienic details.

Latent Gastric Hemorrhages. J. Boas¹ has examined the gastric filtrate for the presence of blood by means of the guaiac test as modified by Weber,² in a great number of patients, and was struck by its frequent discovery in cancer of the stomach. Boas believes that the presence of blood may be of importance as a diagnostic aid of cancer of the stomach.

Carcinoma of the Posterior Wall of the Stomach. A. Vander Veer³ has performed several operations for the palliative treatment of malignant growths situated at the posterior wall of the stomach. He believes that :

1. In all cases of continued gastric disturbances that do not yield to medical treatment a careful examination and experiment should be made as to the possibility of malignancy being present.

2. Whether a positive diagnosis of malignancy is made or not, the patient continuing to emaciate, suffering more and more, an exploration should be done, and if there is no malignant growth a gastro-intestinal anastomosis should be made.

3. Malignant growths in the posterior wall of the stomach are certainly more difficult of diagnosis, and sometimes escape the notice of the most careful diagnostician.

4. When we have made an exploratory incision, and the growth is found to be in the posterior wall of the stomach, malignant in character, with no possibility of removal by resection or otherwise, although quite deep, yet we should not refuse our patient the benefit of a gastro-intestinal anastomosis.

5. In all of these cases the blood should be carefully examined, as part of the history of the patient, in order to learn of such conditions as may have a bearing upon the nature of the growth.

Primary Sarcoma of the Stomach. Lately the opinion has been steadily gaining ground that many of the neoplasms of the stomach which have hitherto been regarded as carcinomata are really sarcomatous in character. W. S. Fenwick,⁴ of London, has recently written a very important paper on this subject. According to Fenwick, it is highly probable that sarcoma of the stomach constitutes from 5 to 8 per cent. of all primary neoplasms of this organ.

¹ Deutsche med. Wochenschrift, May 16, 1901.

² Berliner klinische Wochenschrift, 1893, No. 19.

³ New York Medical Journal, March 2, 1901.

⁴ Lancet, February 16, 1901.

There are as yet but few facts which bear directly upon the etiology of the disease. According to Fenwick, the round-cell sarcoma seems to affect both sexes with equal frequency and to develop at any age. Nevertheless, there is a distinct tendency for it to occur at an earlier period of life than carcinoma, since the mean age of twenty-nine cases was only thirty-four years. The spindle-cell variety, on the other hand, is five times as frequent in women as in men, the average age of the collected cases at the time of death being fifty-one years.

The general symptoms of sarcoma of the stomach are essentially the same as those which accompany other forms of malignant disease. One of its earliest and most striking features is progressive emaciation, with failure of physical power. This is usually most conspicuous in young persons and in cases where the growth causes early contraction of the pyloric orifice. When the neoplasm only affects a comparatively small portion of the viscus, as in the spindle-cell and myosarcomata, the loss of flesh is chiefly observed in the later stages of the complaint or after ulceration has taken place. Anæmia is always present, and gradually becomes profound, but if there is continued fever or repeated hemorrhage its progress is very rapid. It is characterized by a great diminution both of hæmoglobin and red corpuscles. Fever is occasionally observed, as is also albuminuria.

A palpable tumor connected with the stomach is an inconstant sign of round-cell sarcoma, and was only observed in about 30 per cent. of the recorded cases. In most instances it is produced by a local thickening of the gastric wall in the region of the pylorus, and was described as a round or oval mass, occupying the right hypochondriac or epigastric region, smooth on the surface, somewhat tender upon pressure, and often freely movable. Rapid increase in size can sometimes be observed. In other instances the tumor consists of the entire stomach, and more than once the concomitant enlargement of the spleen has been mistaken for a malignant mass. In the fibrosarcomata and myosarcomata a tumor is almost always present and is often so large as to occupy the greater part of the abdominal cavity. If the growth is situated near the great curvature it is usually detected in the umbilical left hypochondriac or lumbar region, where it forms a smooth, firm, painless mass which is dull on percussion and freely movable in all directions. This latter peculiarity affords a marked contrast to the behavior of a carcinomatous growth in the same position, which is invariably fixed by extensive adhesions to the neighboring viscera. The chemical analysis of the gastric contents in sarcoma of the stomach does not differ much from that found in cancer.

With regard to the differentiation between sarcoma and carcinoma of the stomach, Fenwick gives the following points: "(1) The disease

usually occurs before thirty-five years of age, so that the younger the patient the greater the probability that the malignant affection is sarcomatous in character. (2) In many cases there is slight but continuous pyrexia, accompanied by rapid and profound anæmia, while in carcinoma fever is always absent during the early stages of the complaint and the cachexia much more gradual in its development. (3) Simple enlargement of the spleen is by no means infrequent, but is never met with in cancer unless the organ is involved in the growth. (4) According to Kundrat, the tonsils are apt to enlarge and the follicles upon the sides of the tongue may become swollen or ulcerated. (5) Secondary deposits in the skin occur in a notable proportion of the cases and permit of excision and microscopical examination. It should be remembered, however, that sarcomatosis has been met with in true cancer of the stomach (Leube). (6) A large nodular tumor due to infiltration of the omentum, or a greatly enlarged liver with secondary growths in its substance, is rarely met with. (7) Persistent albuminuria is often observed in sarcoma, but is exceptional in cancer. (8) The discovery of pieces of morbid growth in the vomit renders the diagnosis certain (Riegel, Westphalen)."

The treatment will consist in early excision of the growth. There is one case of an operation for sarcoma of the stomach reported in which there was no recurrence of the growth at the end of a year.

Benign Tumors of the Stomach. R. Watanabe¹ describes two cases of benign papillar tumors of the stomach discovered at autopsy. One of these tumors attained the size of an apple, and was situated not far from the pylorus. In each case the tumor mass consisted of an accumulation of glandular and interstitial tissue, and was situated in the mucosa. Watanabe designates these tumors as "papillary fibro-adenoma."

The Condition of the Gastric Functions after Gastro-enterostomy. Charles S. Fisher² has made a series of investigations in four selected cases with regard to the gastric functions (secretion and motility) before and after a gastro-enterostomy. While he almost always found an improvement in the motor function after the operation, the secretion did not seem to change much. In two of the cases (III. and IV.) there was no stricture at the pylorus; in one there was hyperchlorhydria and spasm of the pylorus; in the other atonic dilatation.

It is in this class of cases (III. and IV.) that very definite rules for operating are desirable. The results desired in these cases are remote, not immediate. As these results depend upon the actual condition of

¹ Archiv f. Verdauungskrankh., Band vii. p. 15.

² Medical Record, September 8, 1900.

the mucous membrane at the time of operation, and also the course of the disease for a long time before operation, it now appears desirable to eliminate from the statistics all those cases in which it has not been possible to ascertain the actual structural condition of the mucous membrane of the stomach by repeated analyses for months prior to operation. It is unfortunate, therefore, that we should miss from many of the reports the detailed and serial analyses and observations of the internist before operation, for it is only in this way that a definite knowledge of the actual condition of the mucous membrane can be obtained. A few gastric analyses made immediately before operation are of small value in this respect, especially in neurotic cases. The stomach reacts to the emotions somewhat like a lachrymal gland. It either secretes profusely or very little. It is for this reason that Fisher has come to discard the results obtained by a first analysis of the gastric contents. They are generally erroneous. In most cases repeated analyses at stated intervals and after various meals are necessary to secure sufficiently accurate figures which may be used in diagnosis and prognosis. Especially is this the case, as most of us have not the time to look for nor the courage to scrape off particles of mucous membrane for microscopical examination.

That the results to be obtained by gastro-enterostomy and the prognosis to be given depend upon this knowledge has been sufficiently demonstrated. Whether or not a hyperchlorhydria is to recede after operation depends in a certain proportion of cases upon the structural changes which have taken place in the mucous membrane. It has even been shown that it may increase, and this brings us to the absolutely independent character of the gastric secretions, and the progressive nature of structural changes once begun, even though the cause for the beginning of these changes has been removed by operation. In Cases I. and IV. we have diametrically opposed conditions. In one we have hyperacidity due to cell proliferation, and in the other progressive subacidity due to cell atrophy, and in both the most marked improvement in the general nutrition and local distress; yet in both, one and two years after operation, we find that the abnormal conditions of secretion have progressed in their respective directions. This obstinacy on the part of the secreting cells of the gastric mucous membrane is a matter of common observation in the treatment of a considerable proportion of chronic gastric affections, and continues after the active dyspeptic symptoms have disappeared.

Vertigo Due to Gastric Disturbances. While there is no doubt that vertigo exists frequently as a symptom in organic brain diseases as well as in labyrinthine disorders, there is still some controversy whether vertigo occurs, also being due to gastric ailments. Following

Trousseau and other writers, McCaskey¹ describes a case in which vertigo improved very quickly after ameliorating the gastric condition.

The relationship existing between digestion and the paroxysms of vertigo was so constant as to leave no reasonable doubt as to the causal relationship of the former. Added to this we have the complete disappearance of the vertigo consecutive to stomach treatment. So far as the aural findings are concerned, the case corresponds to a group described by Dr. C. H. Burnett, in which he says the vertigo is the result of chronic catarrhal otitis media. These cases he describes as paroxysmal in character, always associated with tinnitus and a certain grade of deafness, and followed sooner or later by nausea, vomiting, reeling, and falling. It is quite possible, in this case, that without the middle-ear disease the vertigo might not have occurred. It seems equally certain, however, and indeed much more certain, that without the gastric disturbance the vertigo also would not have occurred.

From a clinical point of view, therefore, the stomach must be regarded as a necessary, and possibly an efficient, cause of the severe paroxysmal vertigo present in this case. It is interesting because of the combinations of gastric and middle-ear disease, the probable absence of labyrinthine disease, and the obvious relief of the vertigo as a result of intragastric treatment. In dealing with several hundred cases of chronic gastric disease McCaskey has found a considerable number in which vertigo was a more or less conspicuous symptom, developing *pari passu* with the gastric symptoms and disappearing as they did. As a general rule, however, the vertiginous attacks have not the fulminating character shown by the group of cases commonly designated as Ménière's disease, in which group some writers include the vertigoes of external and middle ear as well as those of internal ear disease. In some of these cases of gastric vertigo, however, the attacks are distinctly cyclic in type. In one recent case the patient fell to the ground on several different occasions, and yet the most critical examinations failed to reveal any cerebral or ear disease.

Gastro-intestinal Fermentation, Indicanuria, and Oxaluria. In an experimental study on the relation of indicanuria and oxaluria to gastro-intestinal fermentation, J. A. Wesner² comes to the following conclusions :

1. Traces of oxalates are found normally in the urine, having been taken in with the food.
2. Oxalate crystals usually denote gastro-intestinal fermentation. Food rich in oxalates must be excluded.

¹ Journal of the American Medical Association, March 23, 1901.

² Ibid., April 6, 1901.

3. Abundance of oxalate crystals does not signify high acid percentage, because in addition there may be oxalate of lime in solution.

4. Indican is often, but not necessarily, associated with oxalate crystals.

5. Hyperacidity on a meat diet contributes to putrefaction, whether due to excess of hydrochloric acids or acids of fermentation.

6. In certain disturbances of the gastro-intestinal tract due to excess of hydrochloric acid or to excess of fatty acids, in which there is fermentation, indican and oxalic acid are increased.

7. The symptoms of oxalic acid diathesis associated with indicanuria are not due to the oxalic acid nor to the indol, but to other products formed in the process of fermentation, and therefore the oxaluria and indicanuria are valuable as indicative of a putrefaction, to which the symptoms are to be referred.

Gastric Secretion in Tuberculosis of the Lungs. Newman¹ has repeatedly examined the gastric secretion in twelve cases of pulmonary tuberculosis, and found the following :

Of seven cases in which the diagnosis of tuberculosis was evident when the patient first came under observation, one case showed hyperchlorhydria. Two cases, which were also probably early cases, showed normal or nearly normal acidity. One, in which the physical signs were slight, showed a total absence of hydrochloric acid, with the presence of organic acids, particularly lactic acid, and marked gastric dilatation. In three advanced cases the acidity was below the normal when first examined, and in the one determination HCl was absent.

Of the cases longest under observation, as the cases progressed the amount of free HCl lessened. This was particularly noticeable in Case I., which showed excessive hydrochloric acid secretion in six examinations, but a total absence of HCl toward the termination of the disease. This may explain the diversity of results obtained by different observers, some having examined early cases, others those advanced. Comparative results, to be valuable, must cover the gastric examinations of the cases from their incipieny to the terminal stage, the progress of the tuberculosis seemingly inducing toward the later stages decrease of HCl or its total absence, even in those which showed early in the disease hyperchlorhydria. As a practical point in the treatment of gastric symptoms, we should not give drugs which increase the HCl secretion, such as *nux vomica* or *capsicum*, or add to it by prescribing HCl dilute, simply because of anorexia or gastric distress, as this is no indication of the absence of hyperchlorhydria, and if it be present we increase the trouble. Newman says :

¹ Albany Medical Annals, May, 1901.

“In some of the advanced cases the stomach contents showed the presence of putrid sputa. In one instance the swallowed sputa, after sedimentation by the centrifuge, was examined and tubercle bacilli were found.

“Einhorn has drawn attention to the evil effects of these swallowed sputa on the gastric mucosa by inducing gastritis, and its sinister effect on digestion, and he emphasizes the necessity of warning phthisical patients against its dangers.”

CONDITION OF THE STOMACH IN EARLY TUBERCULOSIS. Boardman Reed,¹ in a paper entitled “Stomach Conditions in Early Tuberculosis,” emphasizes the following points:

1. In early tuberculosis the secretion of HCl in the stomach is very frequently excessive, the peptic glands being in a condition of irritability which causes stimulant remedies of the creosote class to disagree and act injuriously.

2. Oils tend to depress the secretory function of the stomach, and, in consequence, cod-liver oil is likely to help the cases which the creosote class of drugs hurt; but, on the other hand, hurts the cases in which the gastric secretion is inactive, the very ones in which creosote and the like often do good.

3. Therefore, it ought to be the rule to ascertain the condition of the secretory function of the stomach before pushing either class of remedies.

4. When analysis of the gastric contents cannot be made, it is safer to combine creosote with cod-liver oil, so as to let one neutralize the other in their influence upon the stomach.

5. The motor function is very generally depressed in tuberculosis and must be restored before a cure can be brought about. Drugs avail little in this direction, but diet, exercise, especially in the open air, faradism and abdominal massage—except when hyperchlorhydria complicates—are all valuable means of effecting the result.

Gastroptosis. George R. Lockwood² arrives at the following conclusions with regard to gastroptosis:

1. That in the great majority of cases an adequate cause for the gastroptosis is not discoverable.

2. That gastroptosis does not of itself, in an uncomplicated form, produce symptoms.

3. That the displacement of the stomach, however, is a predisposing cause of a variety of gastric neuroses, of sensation, motion, and secretion.

4. That these neuroses are usually induced by some definite mental or physical strain.

¹ Philadelphia Medical Journal, December 1, 1900.

² Medical Record, December 1, 1900.

5. That the displacement of the stomach is a strong exciting cause for muscular atony; that atony is the most common cause for the symptoms presented.

6. That a complicating atony is associated with a more or less profound neurasthenia, and that a direct relation exists between these two conditions.

7. That gastric acidity is increased in direct proportion to the atony unless counteracted by gastritis.

8. That mild degrees of gastritis are apt to occur in stomachs that are displaced, but the symptoms are neither severe nor persistent.

9. That gastritis occurring in atonic and displaced stomachs reduces the excessive acidity of these cases and seems to modify the severity of the symptoms.

10. That atonic dilatation without mechanical hinderance is exceedingly rare.

11. That dilatation, or, better, muscular insufficiency, may occur in gastroptosis from duodenal kinking, from arterio-mesenteric constriction, or from pyloric spasm.

12. That pyloric spasm is common in displaced atonic stomachs with hyperacidity, and may lead to a temporary dilatation.

13. That in a large number of cases inattention to the condition of atony, of neuroses, and of gastric secretions has led to an unsuitable, insufficient diet, which reacts both on general nutrition and on local conditions within the stomach.

14. That surgical intervention is applicable only to the cases in which dilatation exists.

McPhedran¹ also discusses the subject of gastroptosis. He considers the prognosis good, and illustrates this by the report of cases. He arrives at the following conclusions:

1. Gastroptosis frequently exists without giving rise to any discomfort. So long as the functions of the stomach are performed efficiently no symptoms will arise from its abnormal position.

2. The symptoms of gastroptosis are due to the protracted retention and decomposition of food in the stomach, with the local irritation and constitutional poisoning resulting therefrom.

3. In the condition known as Glénard's disease the gastroptosis or splanchnoptosis plays only a part, often a minor one, in the production of the symptom-group. In not a few instances the splanchnoptosis is rather the result than the cause of the condition.

The conclusions under 2 and 3 cannot be taken as the general view prevailing on the subject. According to my opinion, gastroptosis, as

¹ American Medicine, April 27, 1901.

such, is hardly ever accompanied by retention and decomposition of food. In Glénard's disease the splachnoptosis, while not the only cause, of the symptoms, is certainly essential in producing the morbid manifestations.

Enteroptosis. J. R. Arneill¹ found among 2004 patients 80 cases of enteroptosis, 69 in women and 11 in men. According to Arneill, there is no etiological connection between enteroptosis and chlorosis. Meinert might with as good reason decide that chlorosis caused enteroptosis as the reverse. Most cases of enteroptosis are anæmic, but do not have the special variety of anæmia termed chlorosis. Chlorosis is often met with in persons without enteroptosis, and many enteroptotics do not have chlorosis.

I have also recently published a paper on "Enteroptosis."² The essential symptoms are the following: The patient often complains of a faint feeling or a certain weakness after rising. There is frequently a feeling of considerable fatigue after slight exertion, principally after walking. In women the sensation of fatigue is also combined with pronounced backache. A feeling of weight is occasionally experienced in the lower half of the abdominal cavity, while a dragging sensation is felt in the epigastric region. Flatulence is often encountered, constipation is present in most of the cases, and frequent micturition in a considerable number. Aside from these direct symptoms, it is safe to say that any disease of the digestive tract complicating enteroptosis does not show the same tendency to yield to the usual remedies as normally. The abnormal position of the abdominal viscera produces a weakening effect upon the resisting power of the organism and its energy in combating maladies, especially when the latter exist in them. This explains why the greater part of patients with enteroptosis are troubled with one or the other variety of stomach or bowel disorder, or both. Cases of enteroptosis, lasting a long period, frequently lead to pronounced anæmia, in consequence of subnutrition. The latter gives rise to a host of nervous manifestations (neurasthenia).

Patients with enteroptosis are, as a rule, thin and slender, and often appear younger than they really are. The abdominal walls are generally flaccid, and the abdominal cavity appears to be too commodious for its contents. Palpation is extremely easily executed in these patients, there being, as a rule, no rigidity of the muscles. When the patient stands, the lower part of the abdomen shows a round protrusion, which begins at the navel, while the epigastric region presents a caved-in appearance. This is principally found in female patients. In the

¹ American Journal of the Medical Sciences, April, 1901.

² Medical Record, April 13, 1901.

latter, a pendulous abdomen may be encountered, especially in patients who have had children. In the same class of patients diastases of the recti muscles are occasionally met with.

The stomach occupies a low position—gastroptosis—that means the greater as well as the lesser curvature has been pushed downward. The abnormal position of the stomach can be easily demonstrated by the following three procedures :

1. Splashing sound. 2. Inflation of the stomach with gas. 3. Gastrodiaphany. The most convenient and easiest means is the splashing sound. On tapping, principally upon the left side of the abdomen below the margin of the ribs, in a partly filled condition of the stomach, there will be no sound audible immediately below the ribs, while somewhat further down in the region of the navel, above and below it, the splashing can be distinctly heard. The area over which this splash can be produced will indicate the position of the stomach. Inflation of the stomach with gas, as well as gastrodiaphany, will certainly distinctly show the descent of the stomach ; but these procedures, being a little more complicated, will be reserved for doubtful cases.

Strong pulsation of the abdominal aorta is frequently encountered, and is probably due to the partial uncovering of this vessel by the slipping down of the stomach. The transverse colon, the cæcum, and part of the ascending colon, as well as the sigmoid flexure, can often be distinctly palpated. The transverse colon is frequently found in these cases as a ribbon-like body running horizontally above the navel.

The right kidney is often found movable, occasionally both kidneys are, seldom the left kidney and the spleen. The liver may also partly or wholly descend, and thus a more or less considerable surface of this organ will be accessible to palpation. In females a prolapse of the uterus is not infrequently found. Apparent tumors of the abdomen are occasionally encountered in patients with enteroptosis. The method of examination for movable kidneys and floating liver is well known, and can also be found described in my previous papers.

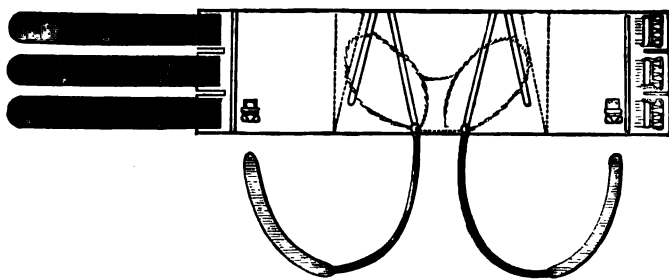
DIAGNOSIS. The diagnosis of enteroptosis is quite easy. It is only necessary to think of this condition, and it is not likely to escape detection. The subjective symptoms above detailed, in conjunction with the result of a thorough examination of the abdomen by the usual physical methods, will reveal the presence of enteroptosis. Another auxiliary in diagnosis of this condition is the so-called Glénard's "belt test." The physician, standing behind the patient, encircles the lower part of the abdomen of the latter with both his hands, at the same time supporting and partly lifting it. The patient is now asked if this procedure gives him relief. If so, it speaks in favor of the presence of enteroptosis.

PROGNOSIS. The prognosis of enteroptosis is good. When appropriate treatment is instituted an amelioration in the condition of the patient quickly takes place. Whether a full *restitutio ad integrum* can take place is not yet definitely settled.

From my own experience I would say that a perfect cure of enteroptosis is possible. I know of positive cures—that is to say, the stomach has returned to its normal position, and a movable kidney has disappeared—in more than a dozen cases of my own.

TREATMENT. The principal part in the treatment of these cases consists in the application of a well-fitting abdominal supporter, ample nutrition, and exercise. The bandage should support and partly lift the lower part of the abdomen. The accompanying illustrations show various abdominal supporters commonly used. It is immaterial what kind of a bandage is used if it only fulfils the above purpose. The bandage should be provided with windows over the iliac crests, also with straps

FIG. 1.



Glénard's bandage.

at the thighs, which prevent its slipping up. Special pads for a movable kidney or a floating liver are, according to my opinion, of no value. A. Rose recommended the use of adhesive plaster over the lower part of the abdomen, instead of the bandage. In some instances this procedure may be tried.

Ample nutrition is certainly important, perhaps more so than the bandage. This must be effected by all means. The diet may, in instances in which the condition of the gastric secretion is known, be adapted more or less to it. But this is not so essential as the knowledge that we should make our patients eat more than is absolutely necessary for the maintenance of the balance of the body. As a rule, frequent meals, plenty of bread and butter, good, plain food, with no very indigestible substances, are indicated. I usually have the patients take milk, and bread and butter between meals. In this regard I differ somewhat from Glénard, who is of the opinion that milk is especially harmful in this class of patients.

Exercise is another important factor in strengthening the constitution generally, and the abdominal muscles particularly. Out-door sports seem to be especially adapted for this purpose. Massage has also been warmly recommended. According to my opinion, however, this is of value only in cases with mild enteroptosis, but not in greatly anæmic patients, or in the advanced cases, for it often creates too much irritation, and may even give rise to inflammatory processes in the abdominal cavity, especially if vigorously executed.

Electricity seems to be especially adapted, when administered intra-gastrically, to cases in which there are manifold functional disturbances of the stomach.

FIG. 2.



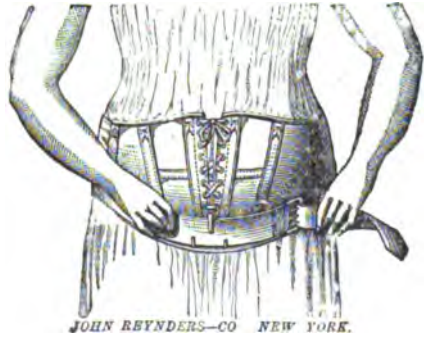
Bandage with holes over the iliac crests, and straps around the legs, as generally used by the writer.

FIG. 3.



Empire abdominal support.

FIG. 4.



Teufel's abdominal supporter.

Of medicaments, iron and arsenic are often indicated in anæmic conditions, while the bromides may be given to allay great nervousness. All the digestive disturbances should be managed according to the general rules. This applies also to the constipation which is so frequently found in enteroptosis. Too many laxatives, however, should not be given, nor is there any need of a laxative treatment in cases in which regular movements are present.

Apparent Tumors of the Abdomen. I have reported a number of cases of apparent tumors of the abdomen.¹ These tumors relate to

¹ Medical Record, November 24, 1900.

swellings found either directly in the epigastrium or the left or right hypochondrium, and have nothing to do with a neoplasm of whatever kind. (I have purposely avoided the expression "phantom tumor," as the latter is usually applied to tumefactions occurring principally in the lower part of the abdomen in hysterical subjects, and caused by a high degree of meteorism. With these our cases have nothing in common.)

In most cases of this kind a resistance may be detected by palpation, sometimes even by inspection, lying between the ensiform process and the umbilicus, presenting a rather smooth surface and frequently pulsating. The size of these tumefactions varies between that of a hen's egg and a man's fist. Light percussion always elicits a dull sound over the area of resistance.

In the cases described by me there was apparently a tumor in the upper half of the abdomen, which could easily have been mistaken for a neoplasm. We now naturally ask ourselves how this apparent tumor is produced. The apparent tumor may be produced: (1) By a prolapse of the left lobe of the liver; (2) by exposure and thickening of the abdominal aorta; (3) by a hypertrophic condition of parts of the abdominal muscles; (4) by adhesions (?) around the smaller curvature of the stomach.

DIAGNOSIS. In apparent tumors the swelling presents a more or less smooth surface; at all events there are no distinct nodules. The tumor is not always felt with the same degree of distinctness, and sometimes may escape palpation altogether. The tumor occupies the position described above, and a high degree of enteroptosis is usually associated with it. As further aids to diagnosis we have the course of the disease, which usually extends over years; the age (it may occur from the time of adolescence to old age), and the malnutrition, which generally is not of recent date but has lasted for a long time. If all these points are present together, the distinction from a real, malignant neoplasm is easy. Cases, however, occur in which the differential diagnosis is not so easy. In the first place, real neoplasms may at times present some of the characteristics of apparent tumors (*i. e.*, a smooth surface or an elongated shape, etc.); on the other hand, apparent tumors may simulate the characteristic appearance of carcinoma. Thus there may be a rapidly progressing emaciation, as in a case mentioned in my paper, and other facts pointing more to carcinoma may be present, and yet we have to deal with only an apparent tumor.

In general, the diagnosis of apparent tumor is easy. There are, however, exceptional cases in which the decision, whether we have a real neoplasm before us or not, is exceedingly difficult. In these latter

cases there is nothing left for us to do but to wait some time. Observation extending over a few weeks or months will then decide this question. In a neoplasm changes will occur (the swelling grows, the symptoms become worse), whereas an apparent tumor remains unchanged, or its symptoms rapidly diminish under suitable treatment.

Concerning the *etiology* of apparent tumors, it is evident that they occur principally with pronounced enteroptosis. Great emaciation and the removal of certain abdominal organs (uterus, ovaries, etc.), which are of such great importance in the development and increase of enteroptosis, are also important factors in the development of the picture of apparent tumor.

As to *treatment*, it is hardly necessary to remark that the apparent tumor itself does not need any curative measures. The original disease must be determined and treated according to rational methods. Two points, however, are to be observed in the treatment of all these cases: First, the attention of the patient must be diverted from the existence of the tumor, or the patient's mind must be assured; secondly, sufficient nourishment must be prescribed and must be persisted in. In a great number of these patients sitophobia is present, and this must be overcome according to the principles laid down in my article on the diet of dyspeptics.¹

If both these indications are thoroughly met the main object has been accomplished, and a favorable result will soon follow.

THE INTESTINES.

Perforating Ulcer of the Duodenum. Robert F. Weir² reports the following case of perforation of a duodenal ulcer, with operation: Man, aged thirty years, who had symptoms, for several months, confusedly detailed, of gastric disturbance, but not of hæmatemesis, was seized four days previously with severe epigastric pain, chill, fever, repeated vomiting and great prostration. No blood was expectorated or dejected. His abdomen rapidly swelled and became generally tender and painful. On entrance into the New York Hospital, April 30, 1899, nothing could be made out by palpation save that the liver dulness was nearly obliterated. The abdomen was very tympanitic, and no special point of tenderness or dulness was observed. He also had a double hernia. On the right side there was a protrusion of intestine beyond the external ring. Pulse 140, temperature 104°. The diagnosis of a general peritonitis from a gastric or duodenal per-

¹ Medical Record, January 1, 1898.

² Boston Medical and Surgical Journal, May 3, 1900.

forating ulcer was made. A large median incision was made, with umbilicus in centre for general exploration. The fingers showed nothing at rings or at cæcum, and then on carrying the examination upward a minute sharply defined perforation, one-fourth inch in diameter, was found on the anterior wall of the duodenum, near the pylorus, out of which was oozing some brandy and water given just before chloroformization. This was sutured with a double row of Lembert sutures and the peritoneal cavity systematically and carefully washed out with sterile salt solution. He was returned to the ward in bad condition. Salt transfusion, 75 ounces, was used, but the patient succumbed shortly after the operation.

The autopsy showed the perforation to be in the duodenum just below the pyloric termination and in its superior anterior wall. Within the bowel was a deep ulcer, at the bottom of which had occurred the perforation.

Antiperistaltic Movements of the Intestines. Bernheim¹ has made an extensive study with regard to the views of Grützner, Swiezynski, and Riegel that there exist even in the normal condition antiperistaltic movements of the intestines. The result of Bernheim's experiments may be put down as positive in the meaning of the named clinicians. In this matter we can better understand the good effect of the nutritive enemas, especially when we consider cases in which patients have been nourished exclusively by rectal feeding, not only for days or weeks—among others, Donkin, up to twenty-three days; Boas, up to fourteen days; D. D. Stewart, twenty-three days; the writer, eleven days—but also for months—Leube, six, and Riegel ten months. The occasions of temporarily suspending the ingestion of food into the stomach are not too rare, particularly in cases of stenosis of the œsophagus, cardia, and pylorus, gastric ulceration and hemorrhage, certain poisonings, when the mucous membranes are destroyed, gastric hyperirritation and dilatation of the stomach; beside these, rectal injections can be effectively used as carriers of medicine in cases of intestinal affections.

Common Anomalies of the Colon. W. W. Babcock² has studied in autopsies the position of the colon and found it frequently abnormal. In the 7 cases Babcock reports the anomalies were as follows: Case I. Anomalous course of the first portion of the ascending colon. Unusual course and dilatation of the omega loop. Case II. Elongation and displacement of the sigmoid flexure. Case III. The sigmoid loop touches the lower border of the left kidney. Case IV. Exaggerated

¹ Journal of the American Medical Association, February 16, 1901.

² International Medical Magazine, March, 1901.

and displaced sigmoid loop. Case V. V-shaped course of the transverse colon. Case VI. Exaggerated V-shaped course of the transverse colon. Case VII. Anomalous direction of the transverse colon. The illustrations given by the writer are excellent. According to Babcock the transverse colon is subject to wide variations in length, and considering its lax attachments it is not surprising that deviations from its usual transverse course are common. The cæcum shows deviations in position and direction more frequently than does the ascending colon, while congenital anomalies of the descending colon are practically never seen.

Displacements or elongations of portions of the colon may also be the result of acquired causes, such as the overloading or overdistention of the bowel, the traction resulting from adhesions, and the pressure from displaced or enlarged organs or from tumors. In none of the cases here recorded which illustrate common types of deviation in the course of the colon was such an acquired cause apparent. In no case was the condition diagnosed during life, nor was it evident that the lesion of the colon was in any case responsible for the fatal result. The frequent occurrence of these anomalies is shown by the fact that the seven well-marked cases here described occurred in thirty consecutive necropsies which Babcock held at the Philadelphia Hospital during November and December, 1900. Indeed, marked deviations from the usual course of the colon are so common and so frequently without very evident symptoms that it is not improbable that a portion of the reported cases of severe abdominal disorder attributed to this cause may have been founded upon a coincidence rather than a true etiological relation. Conversely, it is probable that obstinate constipation, tympany and other abdominal symptoms of obscure etiology may depend in quite a number of cases upon the elongation, displacement, or tortuous course of portions of the colon.

Appendicitis. The difference of opinion with regard to operative intervention in appendicitis is still unsettled. The majority of physicians and surgeons will, however, agree more or less with the views entertained by John B. Murphy,¹ of Chicago. This well-known surgeon excludes appendicular colic and catarrhal appendicitis as not requiring surgical aid and dwells principally upon acute virulent infective appendicitis or shorter acute infective appendicitis. Murphy at first broaches the subject whether a diagnosis of infective appendicitis can be made early, and also whether the course of the pathological changes are discernible. He expresses himself as follows: "One thing we can tell, and I speak very forcibly on this point, namely, that the train of symptoms

¹ Chicago Clinic, August, 1900.

in the beginning is so typical that we can make an absolute diagnosis inside of the first twenty-four hours ; that at the time when we are able to make an absolute diagnosis the infective and dangerous material is still circumscribed by the wall of the appendix. Let us wait another twenty-four hours and make it forty-eight hours ; can we tell at the end of this time the pathological conditions from the symptoms ? No. We can still probably make the diagnosis if we have a fair statement of the case from the beginning, but we cannot say, from the symptoms manifested, that the case is progressing toward a favorable or unfavorable termination.

“In many of the cases we are wofully disappointed in our opinions as to the pathological conditions that exist in the abdomen from the symptoms produced, and I speak of the symptoms that are present in this order : First, pain. This symptom has a significance in making the diagnosis. The pain has a significance on account of its intensity. It is of a colicky character, and we have all the various changes which were so excellently brought out in a paper by Dr. Lee. But can we say from the character of the pain when the appendicitis ceases to be circumscribed by the wall of the appendix, and when it becomes a peri-appendicular abscess ? Theoretically, yes ; practically, no. Can we say that the appendix is or is not perforated at the end of forty-eight hours from the symptoms ? No. Can we say from the symptoms that the case is going in a favorable direction ? No. The symptoms may subside—that is, the pulse may be as low as 84 ; the temperature may be as low as 99° ; the pain may have entirely disappeared and the patient's appendix be completely gangrenous without adhesions. That is what we may expect when we consider a dead appendix which does not undergo absorption ; a dead appendix does not give pain ; a dead appendix does not adhere to its neighboring viscus. It remains free. At the line of demarcation it will adhere wherever there is an inflammatory exudate, but where it is dead it will not adhere.

“At the end of forty-eight hours we are unable to say, from the subsidence of temperature, the lowering of the pulse, the absence of nausea and vomiting, from the favorable condition of these symptoms, what the pathological condition is in the abdomen.”

This uncertainty of the course the disease is going to take is the strongest point in favor of immediate operation, the more so as the mortality is small in the first twenty-four hours and greatly increases with every hour's delay. Murphy says : “The surgeon who believes he can, the first time he sees a case of appendicitis, make a differential diagnosis of the pathological conditions that are present, and predict those which are going to occur, is mistaken. The surgeon who at the end of twenty-four hours says that he can predict the course a case is

going to take, from the appearance of the patient and the general symptoms manifested, is mistaken. The same holds true of forty-eight hours and of seventy-two hours. After a certain number of days we can, with tolerable certainty, predict the outcome of the case. I believe with most surgeons that we are unable to state in the first twenty-four hours what the course of a case is going to be. I believe every honest man admits that the mortality of appendicitis is greater than 2 per cent. I believe that every competent surgeon thinks that he can operate on a case of appendicitis when the disease is still confined to the wall of the appendix, and that he can do so with a mortality of 2 per cent. or less. Therefore, my conclusion is that we are not justified in holding a single case of appendicitis beyond the first twenty-four hours after the diagnosis is made, and it is my belief that, in an enormous percentage of the cases, the diagnosis can be made as absolutely in the first twenty-four hours as it can at any other time."

Robert Abbe¹ has read a very important paper on the problems of appendicitis before the New York Academy of Medicine. He has collected a great number of appendices which have all been treated by first distending them with alcohol and hardening them in it; then cutting them lengthwise, thereby demonstrating the tightness and number of strictures, the pocketing of the appendix, and the condition of the contained stone in view. The resulting demonstration is of the utmost interest. One can see most graphically the cause of all symptoms. In the first series, for example, there are "single strictures," near the colon in one, near the distant end in another. All are quite tight, permitting only a bristle to pass. In one only of the single strictures, which have been removed for the attacks they have caused, is the size reduced to but a third of the normal calibre, and that gave serious trouble because the distention of a six-months' pregnancy bent the appendix and closed the stricture, producing for a time mild septic symptoms.

There are others with multiple strictures, each tight enough to permit alcohol to pass through and distend the next cavity in the appendix, so that five or six successive strictures and channels are seen. When removed from the body these pockets contain mucopurulent fluid, sometimes pure yellow pus, full of infectious bacteria. The colon bacillus is always present, and by authorities is considered the most virulent. The symptoms dependent upon this pathological finding are more apt to be found in the recurrent variety, alternating between a severe colic, with slight fever and an attack of so-called indigestion, with three or four days' detention at home. Indeed, it is this, more than other forms, that is found in patients reduced to chronic dyspepsia and invalidism.

¹ Medical Record, February 16, 1901.

Another series exists in which concretions have formed. Many have been found in the cases of interval operation, but more are removed in the acute, grave, septic cases, in which fortune has brought the patient to operation in the first two days before destructive processes culminate.

The ever-present bacterial activity reduces the morbid effete material within the appendix to a condition capable of expulsion into the colon, or of absorption; so bacterial action, ever going on around the rootlets and sacs of the great trees and plants, breaks up and prepares nutrition for absorption from nature's mould and refuse in the earth.

The ulcerations distinctly visible in the appendix, with points of entrance for poison, are ample evidence of the cause of slight septic fever accompanying the attack for which they were removed. In some the ulcer is a ring-like furrow, half-way or two-thirds around the tube, and, if they progressed to healing, would have in time resulted in linear strictures. It is capable of demonstration that an appendix once thus diseased does not again restore itself to normal health, because of its internal deformity. The detention of its contents, when once a stricture begins to form, converts it, as it has been aptly said, into a veritable culture tube.

The diagnosis is sometimes very difficult. The manner of the appendix of hiding itself from suspicion is nowhere better shown than in conditions of profound pyæmia, into which a patient may be plunged after a day of appendicular disturbance, followed by an absolutely painless condition when the physician is called on the second or third day. Then, perhaps, the patient has a chill, and profound pyæmia, followed by graver and graver symptoms. The physician is justifiably in doubt of a cause, on account, incredible as it may seem, of the absence of local signs, although a septic phlebitis of the larger veins adjacent to the appendix is present. Several times Abbe has witnessed this local peritoneal anæsthesia masking the real cause of fatal pyæmia.

The resemblance of appendicular disease to a large number of internal troubles should afford a chapter in surgery of great importance to the student.

The mimicry of other diseases by appendicular disturbances is so accurate, at times, that the physician has to suspect this complication, not only in any case of supposed gallstone pain, in that of a movable kidney, in that associated with progressive dysmenorrhœa, but he must regard the ordinary colic or the recurrent pains of indigestion to which the "chronic dyspeptic" is subject, as surely due, in many cases, to this cause.

Abbe closes his address with the following words: "I have shown that inflammatory strictures are almost universally present, the foundation and cause of the subsequent disease; that while they are uniformly

of slow growth the real mischief does not begin until occlusion occurs ; that attacks are often cured by natural method ; that a long respite does not mean a cure ; that it is impossible to predict a cure ; that, unless the appendix is out, the disease is always 'latent,' when once it has begun."

Robert T. Morris¹ makes a strong plea for immediate operation in every case in which the diagnosis of appendicitis has been made.

Wheaton² urges the importance of immediate operation in cases of *fulminating appendicitis*. With regard to the recognition of this condition Wheaton lays stress on a new symptom which he has observed in nearly all his cases. It is an apparent vasomotor paralysis, which brings about a cyanosis of the trunk, notably of the abdominal region. It is, of course, only one of the expressions of a condition of shock which follows perforation and a general abdominal infection. In his experience it is present in varying degrees in all cases. If in a given instance the patient is allowed to go to his death it precedes the grand finale but a few hours. It deepens until it becomes general, and we have the general cyanosis of rapidly deepening color, the leaky skin, the incoherence of faulty cerebration, and a speedy and merciful release from the suffering. In proportion as this cyanosis is pronounced or indistinct, it is possible to express with reasonable assurance the probable malignancy of the infection. Any acute attack of pain in the right iliac fossa, in the so-called McBurney region, associated with rigidity of the abdominal muscles, attended either with or without chill and a temperature of 102° and a pulse of 100 or more, should be watched constantly and with the most anxious solicitude ; and if these symptoms increase in severity as the hours go by, every hour of delay in the application of the knife is in Wheaton's judgment a cruel injustice to the sufferer.

Every case of so-called "fulminating appendicitis" should be operated upon as soon as its distinctive characteristics are known. High temperature and high pulse associated with local pain and rigidity are strong presumptive evidences of malignancy in the attack, and if associated with the vasomotor disturbances before referred to, are practically proof positive of the condition of perforation.

TREATMENT OF APPENDICITIS. H. M. Taylor,³ in discussing the subject of conservatism in the treatment of appendicitis, makes a strong plea for surgical intervention. He thus expresses himself :

"What is conserved by medical treatment? An operation for the time being possibly, not probably for all time, is avoided. We say not

¹ Gaillard's Medical Journal, August, 1900.

² St. Paul Medical Journal, November, 1900.

³ Virginia Medical Semi-Monthly, July 27, 1900.

probably, for we think we are within bounds when we claim that 50 per cent. will recur, and later will need an operation. A useless organ is saved, but one which few will deny is far better out of the abdomen than in it, and certainly its retention after once having been infected and damaged structurally is for all time a serious menace to life, health, and usefulness."

Taylor describes several instances in which after an apparent cure of an acute attack of appendicitis symptoms of a chronic nature developed in the appendicular region. They had to be ultimately overcome by surgery. He says:

"Such instances of prolonged suffering and persistent danger warn us that we can never say when a patient is cured after having had one or more attacks of appendicitis and treated only medically. It would seem that the sum total of suffering and loss from work or pleasure is vastly greater in such cases than would result from an early appendectomy. And if we recall that many such cases die without operation, credited to inflammation of the bowels, obstruction, stomach, and hepatic troubles, etc., without the causative influence of appendicitis being appreciated, we must credit the medical treatment of appendicitis and its consequences with more deaths than is usually done. Such instances as I have noted are by no means exceptional occurrences. Surgeons have so often cured intestinal indigestion by removing damaged appendices that such events are no longer unique. .

"As our diagnostic powers increase we eliminate more and more frequently cases from the vague field of functional gastro-intestinal disturbances, and indict inflammatory conditions and their sequences occurring in the appendicular or bile tract regions, and we prove the correctness of such indictment by operation and microscopical and macroscopical findings.

"It is claimed that 75 per cent. of cases treated medically recur and call for constant medical supervision, or else later an operation. While it is well known that the number of attacks is no index to the extent of the adhesions—as in one attack we may have extensive matting, and, on the other hand, many attacks with but little local damage—each attack predisposes to a renewal of the attacks and to the formation of adhesions, and, finally, makes the operation more difficult. In the surgery of the appendix, the ounce of prevention is far better than the pound of cure, and conservative surgery is by no means a synonym for delayed intervention."

S. Lloyd¹ represents a similar view, and is a strong advocate of operating in appendicitis. His own statistics show 160 appendectomies with 4 deaths—2.62 per cent.

¹ Philadelphia Medical Journal, September 29, 1900.

PAIN IN APPENDICITIS. In a paper on "The Significance of Pain in Appendicitis," E. H. Lee¹ arrives at the following conclusions:

1. That in appendicitis, as well as in other abdominal lesions, the pain in the early stage of the disease is of a colicky nature and due to an acute distention of the organ affected; that the greater the distention the greater the pain.

2. That as soon as the acute constriction or distention has subsided or the obstruction has been relieved, these reflex colicky pains and nausea and vomiting cease, and that the pains that are present after this time are of a steady character. They should be described more as a tenderness in the right iliac fossa, and are due to the circumscribed peritonitis.

3. That this last-mentioned pain gradually subsides as the disease progresses toward its favorable termination, either by a perforation of the abscess into the bowel or possibly by the absorption of the circumscribed inflammatory process.

THE DIAGNOSIS OF SUPPURATIVE APPENDICITIS. A. Robin² discusses the difficulty of differential diagnosis between catarrhal and suppurative appendicitis. He lays most stress upon the results obtained by a blood count showing an increase of the leucocytes. In several cases of Robin the hyperleucocytosis was the only sign indicating the suppurative nature of the disease, and at the operation it was found to be true.

It appears rational, therefore, that a frequent blood count in cases of appendicitis is almost an imperative necessity. Robin says frequent, because in some fulminant cases the advent of fatal toxæmia may be so rapid that no increase of leucocytes is present. This is fully in accord with the experiments on animals performed by Havet, who has shown that whenever the dose of staphylococci injected was very large, the ability of the organism to produce leucocytes was proportionally abolished, and instead of the usual hyperleucocytosis a hypoleucocytosis took place. Similar observations were made by Everard, Demoor, Schultz, and others. Cabot reports four cases of appendicitis, with general purulent peritonitis, in which no hyperleucocytosis was found. When, however, examinations are made frequently such mistakes would in the majority of cases be avoided, for we could always detect the hyperleucocytosis before the organism would become sufficiently depressed to fail to react. With all these facts before us we can hardly fail to appreciate the important rôle a blood count plays in the diagnosis of suppurative appendicitis.

APPENDICITIS AND TYPHOID FEVER. H. A. Hare³ describes two groups of cases, viz.: (1) Cases in which symptoms, developing in the

¹ Chicago Clinic, October, 1900.

² Medical Record, October 27, 1900.

³ Medical News, July 21, 1900.

neighborhood of the appendix, indicate the rapid development of appendicitis, yet in which these symptoms gradually subside and the patient gradually passes into an attack of typhoid fever, and (2) cases already well advanced in the progress of typhoid fever which develop appendicular symptoms.

Hare discusses several interesting points in regard to these cases. In the first place, it is of interest that in a certain proportion of cases of typhoid fever the illness is ushered in by symptoms which are most marked in the right lower quadrant of the abdomen. Second, the interesting question arises as to the condition of the appendix and caput coli under these conditions. Third, the further question arises as to whether or not operative interference in these cases is necessary, and, if operative procedures are instituted, whether they are advantageous or disadvantageous; and, finally, whether or not there are any conditions present in such cases which will enable us to state that the patient is suffering from a distinctly local lesion or from a general infection by the specific micro-organism of typhoid fever.

In regard to the condition of the caput coli and appendix, it would seem probable that one or two conditions may be present. One of these is that of ordinary appendicitis, due to the pathological conditions which produce this disease, which happens to occur simultaneously with the onset of typhoid fever, and the other is that the case may be one of those in which the early general symptoms are mild, yet the intestinal lesions are marked.

The differential diagnosis is not easy, as there are no definite clinical symptoms to guide us. The greatest aid in diagnosis of these two conditions can be obtained, according to Hare, from an examination of the blood.

From what we know of leucocytosis, we can rest assured that in ordinary cases of appendicitis the white blood-corpuscles will be considerably increased; whereas, on the other hand, it is a well-known fact that in typhoid fever they are not increased. And, therefore, in all probability typhoidal ulceration in the neighborhood of the caput coli, while it might produce the ordinary subjective and objective symptoms of appendicitis, would not show distinct blood changes.

With regard to the question of an operation, Hare expresses himself as follows: "It has generally been held by physicians and surgeons within the last few years that the presence of a rapid pulse, a scaphoid belly wall, distinct muscular resistance, and violent pain are all symptoms demanding operative interference for appendicitis. And I do not think that the mere possibility of the patient being about to pass through an attack of typhoid fever is any reason in itself for refusing the patient operative relief, although I recognize, of course, that the development

of typhoid fever immediately after such an operation is a grave complication."

TUMORS OF THE VERMIFORM APPENDIX. Tumors of the appendix must be considered very rare. Aloysius O. J. Kelly,¹ in an examination of 706 appendices removed by operation by Dr. John B. Deaver at the German Hospital during 1897, 1898, and 1899, encountered three cases of carcinoma and one case of endothelioma of the appendix. No new growths were ever found in any of the appendices that were removed at necropsy.

Especial interest attaches to these four cases because in all the clinical symptoms were those of appendicitis for the relief of which the operations were undertaken. In three, in addition to the new growths, inflammatory alterations were found. In these three cases also the tumor formation was doubtless primary in the appendix; in Case IV. the involvement of the appendix was possibly secondary to a carcinoma elsewhere in the body. The entire absence of mucous membrane in the appendix, however, and the appearances of the carcinomatous cell formations, suggest that the new growth may have arisen in the appendix and subsequently have implicated other structures. It is also worthy of note that in Cases I., II. and III. the tumors were of microscopical size and were not detected by the ordinary macroscopical examination. The youth of two of the patients, who were aged respectively twenty-four years and nineteen years, is also of interest.

Constipation and Diarrhœa Due to Gastric Disorders. This subject, which was broached by me a few years ago, has been recently fully discussed and confirmed in all its points by Sawyer.² He observed cases in which the diarrhœa or constipation were due to anomalies of gastric secretion. They were remedied by adjusting the anomalies found in the stomach (achylia or hyperchlorhydria). Sawyer says:

"I cannot too strongly urge upon the profession the advantage of recognizing in the conditions described the possible causal importance of departure from normal secretory and motor function of the stomach. In a very considerable number of cases drugs will be wholly unnecessary, or at least of minor importance, if the diet is adjusted in accordance with the findings in the case as to the secretion of the stomach. In this way only do we effectively recognize the fact that a large part of the stomach's work is the preparation of food stuff for the more active intestinal process. And in this course is a ready and successful treatment for some of our most trying and, under other methods, disappointing cases."

¹ University Medical Magazine, May, 1900.

² Medical Age, September 10, 1900.

LAVAGE OF THE STOMACH IN HABITUAL CONSTIPATION. C. D. Spivak¹ maintains that gastric lavage may be made use of in the treatment of habitual constipation. Spivak makes the following statements:

1. A certain percentage of individuals suffering from habitual constipation are apt to have a spontaneous movement of the bowels the following day after the stomach has been washed for the first time.
2. The majority of such patients will eventually recover the normal function of their bowels if lavage is continued daily for two or three weeks, and later at greater intervals.
3. The best results are obtained from using cold water, or hot and cold water alternately.
4. The best time for such lavage is one hour before breakfast.

SPASTIC CONSTIPATION. H. Westphalen² discusses this subject at length. Spastic constipation must be considered as a symptom of mostly functional neuroses, in rare instances, also, of an organic lesion of the nervous system. It is caused by an increased excitability of the sensory nerves of the intestines, which produces tonic contractions of the bowels in a reflex manner.

With regard to treatment, Westphalen values hydrotherapeutic measures very highly, while he deprecates massage. The diet should be abundant in cellulose and vegetable matter. Injections of olive oil into the bowel are also greatly beneficial. Westphalen also had good results from the internal administration of small quantities of olive oil taken three times daily. He also recommends for the same purposes the use of bromide of sodium in conjunction with small doses of chloral hydrate.

Sitophobia of Enteric Origin. Under this heading I have described a few cases in which there existed a fear of food on account of some intestinal trouble.³ These cases are by no means rare. Sitophobia of a moderate degree is almost an everyday occurrence in various intestinal disorders.

Sitophobia, no matter what may be its cause, if left to itself is bound to endanger life. A person who habitually is taking an insufficient quantity of nourishment is slowly starving, and if there be no change in the mode of living, starving to death.

It is hardly necessary to dwell upon the symptoms which appear in this state of subnutrition. They are a host and hardly need any comment: general anæmia, and then anæmia of the brain, dizziness, dryness in the throat, extreme fatigue, insomnia, etc. Occasionally I have met with albuminuria, which promptly disappeared upon improving the nutrition.

¹ Journal of the American Medical Association, April 13, 1901.

² Arch. f. Verdauungs-krankh., Bd. vii.

³ Journal of the American Medical Association, June 15, 1901.

Another important feature of sitophobia is the habit which the patient develops of eating minute portions. The condition which has led to sitophobia may have been remedied, and thus the sitophobia as such may not exist any longer, still the acquired habit of eating very little may persist. This certainly can produce the same dangers to life as the original sitophobia.

TREATMENT. The patient must be made to eat sufficient quantities of food, no matter what is the underlying condition causing the sitophobia, and no matter how this is done. Sometimes persuasion alone is sufficient. Occasionally in very pronounced cases of subnutrition an ample diet cannot be adopted at once, but must be arranged gradually, accustoming the patient to more nourishment step by step. In some instances various medicaments will be helpful in carrying out this plan, thus the bromides in nervous conditions, or codeine in painful affections.

Treatment of Chronic Enteritis by Arsenic. L. Kolipinski¹ recommends hypodermic injections of arsenic in the treatment of chronic enteritis, and also in tuberculous enteritis.

As a menstruum for arsenic Kolipinski has chosen normal salt solution (0.5 per cent. sodium chloride). This can be declared practically painless and patients readily submit to its use. The dose of arsenic, of which sodium arsenite is the best and most eligible combination for this purpose, is from one-sixty-fourth to one-thirty-second of a grain of the salt in sixty minims of the fluid.

The injections may be practised once a week in mild cases, bi-weekly in the average, and every day or two in the severer cases.

Kolipinski arrives at the following conclusions :

1. The arsenical injection is safe, painless, and effective.
2. The dose is very small. From one-sixty-fourth to one-thirty-second of a grain of sodium arsenite is sufficient.
3. One, two, or three injections per week will cure the milder cases.
4. Other internal medication is avoided and the patient has no daily routine of dosing.
5. Greater latitude in diet can be allowed without detriment.

Enterocolitis. W. E. Fitch² discusses the treatment of this condition in children and adults. He highly recommends tannopin. The dose is 1 gramme (15 gr.) three or four times daily for adults ; 0.2 to 0.5 gramme (3-8 gr.) administered every three or four hours to children. It must be given freely, three to eight grains (according to the age of the child), suspended in simple syrup, combined with plain chalk mixture. Fitch maintains that tannopin, owing to its freedom from

¹ Medical News, August 11, 1900.

² Virginia Medical Semi Monthly, September 7, 1900.

odor and its perfect and prompt action, is particularly worthy of trial in the treatment of intestinal disorders, as it, unlike other astringent drugs, is not decomposed in the stomach or rendered inert through insoluble combinations in the upper part of the intestinal canal. This objectionable feature with the class of drugs heretofore used as intestinal astringents has been completely eliminated in the preparation of tannopin, which fulfils all the requirements of a true intestinal astringent, and possesses the following advantages: (a) It can be prescribed with efficiency both per mouth and per rectum, according to the following formula: Sterilized water Oj, and aqua calcis ℥j, to be used with a long rectal tube, to wash and clean out the colon. Owing to its superabundance of lymphoid tissue, the colon is essentially absorptive in function, this function being necessary for the rapidly growing infant. When tannopin, thus administered in plain chalk mixture, splits up into its constituent compounds, it is easily absorbed by the inflamed tissue ready to take it up. (b) It is an efficient medicament in all forms of enteritis, colitis, and inflammatory intestinal disorders. (c) It is advisable to continue the use of the drug in small doses for a few days after the bowels appear to have regained their normal function. (d) It is a completely innocuous powder, and can be administered without risk to the smallest infants, in doses of from three to eight grains, four times daily; and to older children and adults from seven to fifteen grains, several times daily. (e) It acts by the tannic acid of the compound combining with albuminous substances, forming albuminates, which causes contraction of the surrounding connective tissue, diminishes reflex activity, and relieves sensibility of the muscular tissue. *Urotropin*, $(\text{CH}_2)_6\text{N}_4$, acts as a disinfectant by inhibiting the septic organisms, and restoring the integrity of the intestinal mucous membrane, stopping short the process of inflammation.

Treatment of Tuberculous Diarrhoea. Tannopin, in 10-grain doses t. i. d., is also recommended by R. L. Daly¹ in the management of tuberculous diarrhoea. Daly reports nine cases of various forms of diarrhoea in which he has applied this remedy with benefit. According to him the drug should be used in diarrhoea of any type—in the acute cases, because it is almost a specific; and in the cases of tuberculous type, not because it is curative, but because of its quality of reducing the number of stools to one-fourth or one-fifth the ordinary number. In some chronic cases, however, we find the symptom completely checked by the use of tannopin in large doses.

Daly considers tannopin of superior value because of its non-toxic

¹ Denver Medical Times, October, 1900.

properties, its peculiar combination, in consequence of which the drug acts directly on the site of disease, and its absence of odor and taste, rendering it an agreeable remedy in the treatment of what may be considered the most discomforting, unpleasant, and, next to pulmonary hemorrhage, the most dangerous symptom of tuberculosis.

Etiology of Dysentery. Simon Flexner¹ is disposed to view tropical dysentery as consisting of a bacillary and amoebic form separable in their early and later stages by their clinical histories, their etiology, and pathological anatomy. Whether epidemic dysentery may have a simpler etiology future studies will be necessary to decide. The view expressed by Shiga, to the effect that the bacillus isolated by him is the cause of the epidemic disease occurring in Japan, may be followed by the establishment of the same organism as the cause of other epidemics. Flexner's observations prove the wide distribution and pathological activities of the organism as well as its relations with a certain class of dysenteries.

Flexner sums up the present knowledge of the cause of dysentery in the following way :

1. No bacterial species yet described as the cause of dysentery has an especial claim to be regarded as the chief micro-organism concerned with the disease.

2. It is unlikely that any bacterial species that is constantly and normally present in the intestine or in the environs of man, except where the disease prevails in an endemic form, can be regarded as a probable cause of epidemic dysentery.

3. The relations of sporadic to epidemic dysentery are so remote that it is improbable that the two diseases are produced by the same organic cause.

4. The pathogenic action of the amoeba coli in many cases of tropical and in certain examples of sporadic dysentery has not been disproved by the discovery of amoebae in the normal intestine and in diseases other than dysentery. While amoebae are commonly present and are concerned in the production of the lesions of subacute and chronic dysentery, they have not thus far been shown to be equally connected with the acute dysenteries, even in the tropics. In the former varieties, bacterial association probably has much influence on the pathogenic powers of the amoebae.

TROPICAL DYSENTERY. Joseph J. Curry,² in a report on the dysenteric diseases of the Philippine Islands, states that the amoebic type occurred

¹ Journal of the American Medical Association, January 5, 1901.

² Boston Medical and Surgical Journal, vol. cxliv., No. 8.

in a little over 66 per cent. of the cases of dysentery which came to autopsy. In several of the cases of acute dysentery which came to autopsy a bacillus identical with that described by Shiga and Flexner was found in the cultures. Curry concludes his report as follows :

"We have observed two distinct types of dysentery in the Philippines, one amœbic dysentery and the other an acute dysentery, in a number of cases of which the bacillus dysenteriae of Shiga occurred. In addition to these two types we have met cases of subacute and chronic dysentery in which neither the amœba coli nor the bacillus dysenteriae was found."

TREATMENT OF TROPICAL DYSENTERIES. Stephen M. Long¹ discusses the treatment of dysentery. In a case of dysentery or diarrhœa a day or two old give an ounce of sulphate of magnesium in half a glass of warm water before breakfast, repeating it the same day if necessary. Calomel, one-sixth, one-quarter, or one-half of a grain, given every hour, until four or six doses have been taken, and followed four hours later with half an ounce of salts, may answer the same purpose, but if there is any doubt as to the cure of the case we can put the patient on another treatment, namely, ipecacuanha. This drug will often succeed if administered in the following manner: Put the patient to bed, and, while his stomach is empty, administer from fifteen to twenty drops of tincture of opium; then, fifteen minutes later, put an ice-bag on his head, apply a mustard plaster on his stomach, and give a hypodermic injection of morphine, one-quarter of a grain (to give him a chance to sleep), and administer not less than forty grains of ipecacuanha by the mouth; at the same time give instructions to the patient or to the nurse that he is to remain quiet on his back for four hours without moving or taking anything by the mouth, and should the saliva increase in the mouth it is not to be swallowed, but to be spit out.

Another important drug is bismuth. The bismuth subnitrate should be given in very large doses. Forty or sixty grains every three or four hours is a very moderate dose, and if bismuth alone is not enough to check the trouble, then comes the mixed treatment, namely, bismuth and opium. This medicine should never be omitted from the list in treating diarrhœas or dysenteries, whether acute or chronic. There are several ways of administering it, as with camphor, ipecacuanha, as in Dover's powder, or with Squibb's mixture, etc. Long gives forty grains of bismuth subnitrate and five grains of Dover's powder, well mixed, every three or four hours, as the case may indicate.

Long has given the use of enemata a fair trial, and found it in some

¹ New York Medical Journal, March 30, 1901.

cases a life-saving treatment. You will now and then come across cases in which all internal medicines will prove a failure, but which enemata will cure. There is some diversity of opinion as to cold or hot water enemata. In a few cases the cold water may be the best; but, generally, the hot should be preferred for the following reasons: First, it is a better solvent than cold water; secondly, it is cleansing, clearing the bowels from slime and mucus; thirdly, it is aseptic; fourthly, it is absorbed by the tissues quickly; and, fifthly, it is well borne by many. As to what medicines can be used with the enemata: Long prefers of all the antiseptics and germicides, silver nitrate, twenty grains to the pint, or quinine for amœbic cases. The bowels of the patient must be first cleaned with a soapsuds enema before administering the medicated enema. The knee-chest or dorsal position can be tried. As to instruments for giving the enema, never use a hard-rubber catheter or the bulb syringe, as, when the ulcers are in the rectal region, alarming results may follow. A rubber bag or fountain syringe with a soft rectal rubber tube attached to it is all that is necessary for the operation.

COLOSTOMY FOR THE CURE OF CHRONIC DYSENTERY. In a patient suffering from chronic dysentery which resisted the usual remedies, W. N. Sullivan¹ had a colostomy performed with a twofold purpose in view: 1. To give rest to the inflamed bowel by preventing the feces from passing over it. 2. To allow a large flushing irrigation of a portion of the bowel which was probably not reached by injections into the rectum.

After having the colostomy established a stream of pyrozone solution—half a pint to the gallon of sterile water—was passed through the large intestine and as the peristalsis operated it passed out by both outlets, the anus and the artificial anus, thus thoroughly flushing the whole of the large intestine. This treatment was continued daily.

Before the operation the patient had a temperature varying from 99° to 104° F., but on May 2d, two days after the operation, it was normal. The pain, which had been excruciating and agonizing, ceased immediately after the first few days, and he began to eat well of a soft diet, including fish. He gained flesh rapidly. He was kept under this treatment from April 30 until August 30, 1900—four months—when the opening was closed and the bowel dropped back into the abdominal cavity. While the patient was in the hospital careful examination of the feces was made, and the amœbæ coli, which were found in large numbers before the operation, disappeared a few days after the operation and could not be demonstrated afterward.

Colostomy for the relief and treatment of chronic dysentery of a grave

¹ Journal of the American Medical Association, December 8, 1900.

nature has been recommended and performed by several writers (Ewald and others), and certainly will prove of benefit in appropriate cases.

Membranous Enteritis. H. Westphalen,¹ in a paper entitled "On the So-called Membranous Enteritis," arrives at the following conclusions :

1. It is impossible to discern in membranous enteritis, as Nothnagel does, two etiologically different groups, namely, cases of "membranous enteritis" proper, in which the main affection consists in a catarrhal condition of the intestine, and cases of mucous colic in which there exists a neurosis of the bowel. All cases of membranous enteritis are caused by the same etiological factor.

2. The formation of the expelled membranes is probably caused by a neurotic hypersecretion of mucus from the bowel.

3. In case there exists merely a secretory neurosis, the mucus excreted appears in an amorphous form.

4. If in addition to the secretory neurosis there exists spastic constipation, the mucus appears in the form of bands.

5. In case the accumulation of mucus is voided under violent pains, there exists, besides, a sensory neurosis.

The treatment, according to Westphalen, consists in all the measures tending to strengthen the nervous system. Hydrotherapy is particularly praised. The diet should be abundant and consist largely of vegetables and fruits. Olive oil enemas are also of benefit, while the drinking of small quantities of olive oil three times daily is likewise beneficial.

Membranous Colitis. John A. Robinson² maintains that a disturbance of the secretory function of the nerves superintending the bowels is the underlying cause of the affection. The disease has a low rate of mortality. It is, however, almost invariably a chronic affection. With regard to treatment, Robinson lays much stress on bowel flushings. When rectal irritation is present the rectum should be washed out with hot water—that is, a temperature of 100° F. In these flushings the soft-rubber rectal tube should be used, as much injury may be done by the use of the rigid tubes. When the patient is suffering from the expulsion of the membranes, the rectal flushings give great relief. Except in severe cases high hot colonic flushings with 1 per cent. solution of boric acid and sodium chloride are very beneficial. These high flushings must be carefully given, by the physician, nurse, or someone specially trained, as undue tension of the bowel must be guarded against. In the secondary forms of the disease it is true that the membranes seldom appear in the stools, but the colonic flushings are just as bene-

¹ Berliner klin. Wochenschrift, 1901, Nos. 14 and 16.

² Medicine, January, 1901.

ficial as in the forms where the membranes are expelled. Letcheff recommends hot solutions of 1 to 1000-2000 of nitrate of silver.

Robinson has also used with great benefit a solution of methylene blue, one grain to a quart of water, by rectal injection, the patient reclining and the injection given high. In using this great care is necessary, on account of the dye so readily staining all clothing.

Intestinal Sand. Some cases of intestinal sand have been observed by C. Georg, Jr.,¹ who has made a thorough investigation with regard to the nature of this sand.

The stools were of a dark-brown color, well formed and normal in consistency. After frequently washing them with water and allowing a sediment to form a number of small grains of pale brown sand, intermingled with a few fine black particles, were found to separate. The amount of sand obtained from each stool was about two drachms by weight. This sand readily sinks in water, and is gritty and hard in consistency. Chemically it contains a small amount of calcium, magnesium, and ammonium. Dr. Novy found a small amount of silica present in this material. The tests for cholesterin and bile pigment were negative. Upon microscopical examination it was found that this sand consisted of isolated groups of thickened vegetable cells closely bound together. There were conical, hexagonal, and irregularly-shaped prolongations from the edges of these groups of cells. It was later determined by Prof. Newcombe that these masses were groups of typical vegetable sclerenchyma. The prolongations were the individual cells separated to some extent from their groups by the dissolving action of the digestive juices. These cells have very thick walls and a very small lumen, caused by the mutual pressure to which they were subjected during growth. It is a form of vegetable tissue which has lost its cellular character, and has been converted into the so-called stone cells by a process of hardening or lignification. These groups of cells form the hard concretions, about the size of a grain of sand, which are found in the soft flesh of the pear. Sclerenchymatous cells are also found in the stones of cherries and plums, pepper, cinnamon, and the tapioca and sago grain. Georg arrives at the conclusion that the organic material which has been found in the majority of the cases reported as intestinal sand is vegetable sclerenchyma. The variety of the sclerenchyma depends on the nature of the food taken in the diet. True intestinal sand, like biliary or renal sand, is formed by a deposit from the secretions of the living body, and consists largely of the salts of lime, magnesium, and ammonium; on the other hand, most of the so-called intestinal sand consists largely of the concretions of vegetable

¹ Physician and Surgeon, May, 1900, p. 225.

sclerenchyma present in the residue of undigested vegetable food, and contains a secondary deposit of a small amount of inorganic salts, including a few silicious particles.

Intussusception of the Bowel in Children. Edward J. Ill¹ describes three cases of intussusception in children in which he operated. The clinical history of these cases is, according to Ill, remarkable for its simplicity. A child, generally of good health, but now and then suffering from intestinal disturbances, colicky in character, is taken suddenly ill with violent pain, usually of intermittent character. Great prostration accompanies this condition, much greater than can be accounted for by a simple indigestion. The face shows great pallor and anxiety, which is marked even in very small children. Tenesmus is not an infrequent symptom, especially when the intussusception is located low down in the large intestine. It is accompanied by discharges of bloody mucus, which in very acute and in severe cases may even be bloody serum or pure blood. We may expect more of this the acuter the intussusception and the lower in the intestinal canal the accident has occurred. In the cases of incomplete obstruction we would not expect much, if any, bloody discharge. The strangulation of the gut being incomplete, its circulation is little disturbed. At first there is no fever, but usually in twenty-four hours there is a gradual increase of temperature. The pulse, contrary to the report of many, has always been rapid in his cases, and showed by its quality the severeness of the injury. Tympanites, which in the early stages is slight, gradually increases until, when peritonitis supervenes, it becomes excessive. We now have the general condition resulting from the ailment. The obstruction is not always complete, and this is, unfortunately, in the eye of the non-surgical practitioner, a good reason for non-operative interference. When the obstruction is not complete nor very acute the symptoms of prostration in regard to facies and pulse are not so marked. The completeness of the obstruction will depend much upon the acuteness of the invagination.

The value and importance of palpating a tumor cannot be overestimated in making a diagnosis. The location of the tumor gives us some idea of the location of the intussusception, but not of the size of the invagination. The tumor was usually of an elongated shape, rather solid to the touch, and somewhat curved. The differentiation is chiefly from that of ordinary colic or a dysentery. The causes of this difficulty are little understood.

Ill maintains that the results by medication and enemata are extremely unsatisfactory, and death is the common result. Until lately it was

¹ American Medical Quarterly, June, 1900, p. 207.

thought that operative interference was likewise exceedingly unsatisfactory. This old opinion must rapidly give way to the more advanced one, that early, prompt, quick, and clean surgery offers the best chances for success. Considering the difficulty Ill has experienced in reducing the invagination with the abdomen open, he has but little respect for the temporizing and useless efforts of posture and enemas. The operation should follow the diagnosis, and the diagnosis should be and can be made by the practitioner at an early hour. Every hour lost increases the risk to the child.

Ill gives the following salient points with regard to the operation: If a tumor is felt the incision should be made in the median line nearest to the mass. In other words, if the tumor is above the navel, the incision should be above the navel; if below the navel, the incision should be there. The space between the navel and pubes is very short, and the incision may have to extend above that landmark. All manipulations should be made in the abdomen itself. It will rarely prove possible to remove the invaginated gut from the cavity of the abdomen. If possible the eyes should follow all movements, so that any injury to the bowel may be promptly repaired. Ill's experience has taught him that the best manipulation is exercised by pressure from the apex of the invagination toward its base. He advises close inspection of the reduced bowel and mesentery for several moments, to observe if there be any tendency to relapse and possible injury during manipulation.

All manipulations should be made with the greatest gentleness. It is hardly necessary to add that there is no room for antiseptics in so tender an organ as the peritoneum of the child. Therefore, all antiseptics should most carefully be washed from the hands, and dry hands should be used for the operation.

A. Primrose¹ has also written on intussusception in children, and entertains very similar views as those of Dr. Ill.

Intestinal Obstruction Due to Gallstones. In the three cases observed by Lowman² there was no fever and no distinct paroxysms of severe pain with intervals of rest. In none was the diagnosis of appendicitis admitted, though suspected. The early fecal vomiting in one proven case spoke for complete obstruction, and justified the belief that the obstruction was a band high in the small intestine. The pain in appendicitis is more continuous, and, unless there is a decided mechanical obstruction, the pain is not so paroxysmal. The obstipation in inflammatory troubles is generally not obstructive but inhibitive. The peris-

¹ Canada Journal of Medicine and Surgery, November, 1900, p. 322.

² Cleveland Journal of Medicine, September, 1900.

talsis is arrested reflexly, the fecal current is stopped by this arrested movement and not by a movable obstacle. There is for some days an increased peristalsis in true obstruction of the bowels, due to nature's attempt to overcome the accident. This in time is followed by paralysis and distention of the bowels. Frequent repetition of severe paroxysmal attacks of pain without fever becomes an important diagnostic point. In such cases when there is a reasonable supposition that there is a movable obstruction at the valve of Bauhin, large hydrostatic enemas should be repeatedly tried. There is a chance that the calculus might be wedged or caught in the long way behind one part of the valve, and that a slight shifting of its position would permit it to slip through the narrow slit-like opening. A large dose of castor oil could accomplish the same result. There is a strong belief that cathartics are harmful in appendicitis. It is well to have it in mind that there are conditions closely simulating appendicitis, and that cathartics are the one thing needful to avert the menacing condition. When doubt lingers and danger threatens laparotomy is imperative.

The Treatment of Ileus by Means of Atropine. In a paper on this subject H. Strauss¹ recommends the use of hypodermic injections of atropine (one to five milligrammes once and even twice daily) in the treatment of acute dynamic ileus. Many successful cures have recently been reported by this heroic treatment. It appears, however, advisable to use smaller doses of the atropine, perhaps one to two milligrammes twice and if necessary (provided there are no symptoms of atropine poisoning) three times daily. Strauss recommends the same plan of treatment in biliary and renal colic.

Rectal Valves and Their Significance. J. R. Pennington² has made an extensive study with regard to the normal and pathological anatomy of the rectum and colon. Pennington's report and other observations show that the plicæ vary as to number, location, size, position, direction, with reference to the axis of the intestine, capacity, and structure. As a rule there are three, sometimes only two; again, there may be four or even more. They are semilunar in shape. Their attachment forms from one-half to two-thirds the circumference of the intestine. Their margins are concave, and they are usually directed slightly upward. They are most prominent when the bowel is distended. Their depth in the adult is from one-half to one inch or more. As a rule the second one is situated, as stated by Kohlrausch, on the right side, opposite the reflection of the peritoneum on to the bladder in the male, or the fornix of the vagina in the female. The other two are on the left side, one above and the other below this one.

¹ Fortschritte der Medicin, 1901, No. 12.

² Chicago Medical Record, December, 1900.

From experimental studies made by Pennington upon the living and the dead, it would seem that the function of these plicae is (1) to prevent the feces from crowding down upon the anus when the bowel is in a passive state; (2) to equalize the pressure of feces that may accumulate in the rectum from time to time, and (3) to facilitate defecation by giving a spiral motion to the fecal mass.

In support of this assumption Pennington submits the following observations:

1. Man is the only animal possessing these structures, and in him they seem to be universally present, and he is the only one that defecates at regular intervals.

2. They are the most prominent when the bowel is distended and occlude quite one-half of the lumen of the rectum.

3. Irritants and foreign bodies cause them to become erect and present or offer as a kind of ledge across the bowel.

4. Their direction, as shown by numerous casts, specimens, and photographs, is slightly upward, forming, in some instances, distinct cups or pockets.

5. The congenital hyperplasia of the mucosa, muscularis mucosa, submucosa, and muscular tunics at their apices or along the free margin of the plica.

6. The binding together of the pillars by white fibrous and yellow elastic tissue.

7. The observations of Gally, that distention of the bowel with water did not efface the valves, as claimed by Sappey and Testut, but augmented the depth of the chambers bound by these structures.

Pennington is also of the opinion that these valves when they are hypertrophied or otherwise in a pathological state may in some instances interfere with normal defecation, and cause obstinate constipation.

CONSTIPATION DUE TO VALVULAR OBSTRUCTION. Thomas C. Martin¹ thus describes the normal action of the rectal valve and also its pathological importance as a cause of constipation. The inflated rectum is from three to four inches in diameter. The normal valve spans about half the circumference of the rectum and projects from one to one and a half inches from the rectal wall, and thus the rectum is divided into a series of chambers. The normal valve is elastic and is gradually effaced under the pressure of the descending feces; it retards the progress of the feces.

Valvular obstruction may be divided into two classes. The first is anatomical, the second pathological.

1. The first is due (*a*) to an embryonic overgrowth of the valve to

¹ Cleveland Journal of Medicine, September, 1900.

such a degree that it constitutes a more or less diaphragmatic obstruction, or (b) the valves have developed from points so propinquitous that the free border of the proximal valve overlaps the free border of the valve next below in such a way that the two conspire to form a temporary diaphragm, which obstructs the descent of the feces.

2. The diseases of the rectal valve are (a) true hypertrophy, which is characterized by a thickening of the valve, and (b) fibrosis, which may be defined as a degeneration of the muscular elements and the formation of fibrous tissue without apparent thickening. The obstruction in these cases is due to rigidity of the valve and not to contraction of the valve-strait. Annular stricture of the rectum is but a very considerable hypertrophy of the rectal valve.

The symptoms of valvular obstipation are abnormal straining at stool for the passage of solid feces. Attempts at defecation do not completely empty the rectum. When the rectosigmoidal valve only is obstructive the patient does not strain at stool; defecation in this case occurs but once in several days, and there is not that unrequited desire for stool which characterizes an obstruction when it is situated in a lower valve.

The commonest complications of the obstructing rectal valve are dilatation and hyperæmia of the sigmoid flexure and colon, membranous proctocolitis, and intestinal auto-intoxication.

The radical cure of these conditions consists, according to Martin, in a valvotomy.

W. Bodenhamer¹ denies the existence of real valves of the rectum. He believes the valves of Martin are merely semilunar ridges of the mucous membrane of the rectum.

THE LIVER.

Tumors of the Liver. R. S. Fowler² discusses the topic of tumors of the liver. He dwells at some length on those of a syphilitic nature. They present two forms, the recent gummata and the botryoid liver, which are the final result of a syphilitic hepatitis. This form has been mentioned in the class in which the entire liver forms the tumor. It presents as an irregular, hard, knobby mass, divided by cicatricial bands. The recent gummata, however, form genuine tumors. They occur as hard nodules or flat masses of large size, presenting most frequently in the epigastrium. They differ decidedly in feeling and shape from the knobs of cancer. In many instances a clear specific history

¹ New York Medical Journal, June 30, 1900.

² Brooklyn Medical Journal, December, 1900.

can be obtained and the diagnosis can be verified by the administration of potassium iodide. While this is unlikely to result in a total disappearance of the tumor, yet there is almost invariably a rapid and marked decrease in size.

Occasionally the abdomen is opened for such tumors when no specific history can be obtained. Such a tumor was exposed by exploratory laparotomy by George R. Fowler in June, 1896, at the Brooklyn Hospital. The patient, a male, aged thirty-nine years, absolutely denied any specific history. He had suffered from pain and distress in the hepatic region for thirteen months prior to his admission to the hospital. During the last month the pain and distress had greatly increased. The liver was much enlarged and was tender. A smooth, hard tumor could be felt just beneath the free border of the right lobe. This was quite tender and resembled a distended gall-bladder. Exploratory laparotomy showed this to be an hypertrophied lobe of the liver. The wound was closed, and under specific treatment the patient fully recovered.

At times gummata break down and find their way to the surface. R. S. Fowler has operated upon one such case in 1898. The patient, a woman, gave a history of hepatic distress extending over a period of months. Examination showed an area of discoloration in the skin just at the right costal border. The liver was much enlarged and there was a history of syphilis. An incision was made through the discolored area and a double handful of broken-down gummatous material was curetted from the interior of the right lobe. The resulting cavity was irrigated and packed with iodoform gauze. Potassium iodide was administered and the patient made a complete recovery.

Abscess of the Liver. W. C. Wood¹ discusses the subject of abscess of the liver; 13 per cent. of tropical abscesses of this organ are latent, giving neither local nor general symptoms until they burst into adjoining organs. Most cases give definite evidence of their presence. The local symptoms are as follows: Rigidity of the upper part of the right rectus muscle is present, this symptom being found in all inflammatory lesions of the underlying structures in the region. Tenderness with slight œdema or even redness is found in advanced cases. The pain varies from a sharp darting one, similar to that of pleurisy, in cases where a perihepatitis is present, to a heavy dull pain in large deep abscesses. There may be no pain where general sepsis is well marked. A localized enlargement of the liver is generally present. There may be a general enlargement in a multiple case, and occasionally the abscess takes the place of destroyed rather than dis-

¹ Brooklyn Medical Journal, December, 1900.

placed tissue, so that no enlargement results. If the abscess is near the upper surface, the liver may be pushed down, or the enlargement recognized only by a thoracic dullness. Here the signs are similar to those of a subphrenic abscess. Very rarely can fluctuation be detected. Jaundice is usually absent, but the complexion is muddy. Reflex pain in the scapular region and a reflex cough or a hiccough with gastric disturbance characterize an abscess in the upper or lower portions respectively. In Southern cases the temperature is said to be intermittent with chills, but here the fever is more constant, although not very high, and rigors are not a marked feature.

The diagnosis of liver abscess is usually easy, but sometimes impossible. Latent abscesses (13 per cent. of tropical cases) cannot be recognized until they burst. Local tenderness with some enlargement, reflex pains, and muddy complexion with an increase of temperature will suggest this infection. The presence of a septic process elsewhere that could have caused the lesion is most important in coming to a conclusion; for it must be remembered that abscess like carcinoma of the liver is practically a secondary lesion. In many cases one cannot decide on the nature of a liver swelling without aspiration.

The prognosis is, according to Wood, most grave. Statistics seem to indicate that 93 per cent. of all cases untreated are fatal. About 10 per cent. rupture into the lung, which is the most favorable termination for a natural cure, as half of these recover, or 5 per cent. of the whole number. A very small number open safely through the skin, and probably a few become encapsulated.

The only rational plan of treatment when the patient is evidently not beyond relief is prompt drainage. Waiting for adhesions to form or for pus to approach the surface of the liver or abdominal wall is more dangerous than early operation. Delay is dangerous in three ways: from septic absorption, from the increase in the extent of liver tissue involved and the number of abscesses, and from rupture.

Bronzed Diabetes. A. P. Condon¹ describes a case of cirrhosis of the liver and of the pancreas, with diabetes and hæmochromatosis, with autopsy. "Bronzed diabetes is a disease characterized by the symptoms of diabetes mellitus, to which has been added a general pigmentation, hypertrophic cirrhosis of the liver, and usually of the pancreas. Bronzing of the skin is usually present, but not in all of the cases. All of the internal organs are more or less pigmented, the liver containing the largest quantity, then pancreas, heart, spleen, kidney, and lungs, the last containing the smallest amount. This pigment gives largely the iron reaction."

¹ Medicine, December, 1900.

Regarding the etiology of bronze diabetes Condon mentions three theories: (1) That bronzed diabetes is a distinct pathological entity—advanced by Marie and supported by Hanot and other French writers; (2) that it is a diabetes mellitus, the diabetic poisons producing the hæmachromatosis, cirrhosis of the liver, pancreas, etc.—advanced by Letulle; (3) that hæmachromatosis is the primary affection, and the deposition of pigment causes the hypertrophic cirrhosis of the liver and pancreas, diabetes resulting when the pancreatitis reaches a certain stage—advanced by Opie.

All authorities agree that the pigment which is deposited throughout the different organs and tissue is largely an iron-containing pigment, but the manner in which this is deposited is still a matter of conjecture.

Destruction of corpuscles in pernicious anæmia, malaria, etc., gives rise to deposit of pigment, but it differs from the pigment formed in hæmachromatosis. Welch suggests that the pigment formed in hæmachromatosis may be due to a specific form of destruction of the red blood-corpuscles.

The Treatment of Gallstones. Riedel¹ gives the following indications for the treatment of gallstones:

A patient having gone through for the first time a successful attack of gallstone colic (developing icterus on the second and third day and passing small stones shortly afterward by the rectum) does not require an operation.

Likewise there is no operation needed if a patient after several unsuccessful attacks of gallstone colic once passes through a thoroughly successful attack with the passage of medium-sized gallstones. In case, however, there is a recurrence of the attacks an operation should be performed.

Whenever there is one unsuccessful attack of gallstone colic without jaundice, there is an indication for operation. The stones should be at once removed before they have a chance to enter into the deeper tissues.

An operation is further imperative in a case in which after many uneventful attacks the stone has been incarcerated in the ductus choledochus.

IMPORTANCE OF EARLY OPERATIONS IN GALLSTONES. W. J. Means² believes that every case should be operated on that presents a train of symptoms indicating trouble in the bile apparatus that cannot be relieved by a course of medicine along the line indicated. It is his judgment, also, based on personal observation, and from the recorded experience of others, that early operative procedure will reduce the

¹ Berliner klin. Wochenschrift, 1901, Nos. 1 and 3.

² Journal of the American Medical Association, December 1, 1900.

mortality of cholelithiasis as much as early operations have reduced the mortality in appendicitis. Procrastination may lead to complications, making an operation quite difficult and dangerous if not impossible.

M. H. Richardson¹ represents the same view in a still more emphatic manner. According to Richardson, the most impressive argument for early operation in biliary calculi lies in the suffering and death which so frequently attend delayed surgical treatment. Even when health is finally restored, it is only after prolonged suffering and illness. In many cases cure is attainable only after repeated, complicated, and dangerous operations. His cases fatal after surgical operations number sixteen. In this list are included every case in which cure has been attempted. Besides these cases there have been six deaths following simple explorations in which nothing was accomplished beyond the demonstration of inoperable malignant disease. There have been several deaths in cases seen too late for operation.

The successful operations number about a hundred. Of these only a small percentage can be classed as early, an early operation being understood to be one performed before secondary changes have taken place in or about the biliary tract, and before the patient's strength has been reduced by the suffering of many attacks of biliary colic. It is only when they are forced by unendurable pain, by jaundice, or by failing strength, that they come under the surgeon's observation. When brought to operation by frequent attacks of biliary colic, without jaundice or loss of strength, the conditions are usually extremely favorable, even if extensive changes are found in the gall-bladder. A large proportion of Richardson's cases of cholecystotomy have been of this class, and the results have been almost invariably good.

D. P. Allen² dwells upon the necessity of early recognition and removal of gallstones. Early operations are desirable because they are eminently successful, while late operations are often, though not always, beset with the gravest difficulties. To diagnosticate gallstones in the presence of the classic symptoms of biliary colic, jaundice, clay-colored stools, bile in the urine, and possibly calculi in the fecal evacuations is, as a rule, easy. It is well, however, to know that all these symptoms, save the presence of calculi in the feces, may result from obstruction caused by chronic inflammatory conditions, even in the absence of biliary calculi. In some cases of advanced disease, due to gallstones, none of what may be called classic symptoms are present.

Allen describes a case in which there were no other symptoms present except pains in the epigastric region, more toward the right side. An

¹ Journal of the American Medical Association, December 1, 1900.

² Cleveland Journal of Medicine, August, 1900.

operation revealed adhesions, almost total obliteration of the cystic duct, and several biliary calculi. Allen arrives at the following conclusions :

1. That in cases of continued distress in the epigastrium, when a physician skilled in modern methods of investigation, both clinical and physical, can make no positive diagnosis and give no relief, an exploratory operation is advisable. How it is to be completed must depend upon what is found.

2. That operation under such conditions frequently results in the removal of gallstones or the setting free of adhesions, and entirely relieving the patient's suffering.

3. That such operations should not be too long delayed, since the formation of dense adhesions, such as are found not infrequently, may greatly enhance the difficulty of operating and endanger the life of the patient.

THE PANCREAS.

Pancreatic Digestion. B. K. Rachford¹ has made extensive experiments on the action of pancreatic juice (obtained from rabbits) on casein. He found that the pancreatic digestion of casein was in every instance slightly facilitated by the presence of a maltose solution, and that a milk sugar solution seemed to exercise the same favorable influence. The inference, therefore, is that rabbits' pancreatic juice in the presence of bile is somewhat assisted in casein proteolysis by the presence of a maltose or milk sugar solution.

In a previous paper Rachford demonstrated the physiological fact that acid proteids undergoing digestion will slightly increase the diastatic action of rabbits' pancreatic juice. It would seem, therefore, from these observations that the inference may be drawn that both the diastatic and proteolytic action of rabbits' pancreatic juice goes on more rapidly when the juice is acting upon a mixture of starches and albumins than when the juice is acting separately upon these food stuffs.

Jacobi has long taught that, in healthy children, milk digestion goes on more satisfactorily when it is mixed with a decoction of one of the cereals ; and most of the recent writers upon the subject of children's feeding have come to agree with Jacobi, believing, as they do, that under the influence of these decoctions the rennet and hydrochloric acid of the stomach precipitate the casein in more flocculent clots, thus enabling the ferments to come in more intimate contact with the casein to be digested. Whatever may be the explanation, however, Rachford thinks we may possibly infer from his experiments that the favorable influence of these cereal decoctions on casein digestion is continued

¹ Archives of Pediatrics, June, 1900.

even after the milk leaves the stomach and comes under the influence of the various digestive enzymes of pancreatic juice in the intestinal canal.

Rachford also found that a small quantity of hydrochloric acid facilitates the action of the pancreatic digestion. In the light of his experiments we can see that the beneficial action of hydrochloric acid is not confined to the stomach, but as combined hydrochloric acid it is continued in the intestinal canal, where it not only aids the pancreatic digestion of casein but also acts as an intestinal antiseptic. It is Rachford's belief that a small portion of hydrochloric acid combined with proteids will, under certain conditions, aid the action of the enzymes of pancreatic juice, while at the same time it exercises a restraining influence on fermentations carried on by organized ferments.

In his experiments Rachford noted at the close of certain experiments that free fat, or butter, was found floating on the surface of all those digestive mixtures in which the milk had been subjected to the action of both bile and pancreatic juice. In other words, it was noted that the physiological emulsion of fats, as it occurs in milk, was partially destroyed by the combined action of bile and pancreatic juice, but that this emulsion was not destroyed by the action of either one of these agents when acting alone. This observation suggests the possibility that the emulsion of fats in milk is wholly or partially destroyed by the action of bile and pancreatic juice in the intestinal canal prior to their absorption. If it be true that the milk emulsion is destroyed in the intestinal canal, and the fats set free, we can readily understand how in certain diseases of the intestinal canal, which interfere with the absorption of foods, we may have, even in milk-fed infants, greasy or fatty stools.

Cyst of Pancreas. A case of multilocular cystoma of the pancreas has been described by Reginald H. Fitz.¹ The patient was a man, aged thirty-six years, with no special previous ailment. In July, 1899, the patient began to complain of a constant dull pain in the left lumbar region, and extending into the dorsal region. It was worse when lying down at night, but was less discomforting when he lay upon his back. The pain gradually increased in severity, until at the end of two or three months it ceased, after the application of tincture of iodine for three or four days. Within the last month he noticed in the left hypochondrium a swelling, which increased a third in size during this time.

Throughout his illness he was not obliged to restrict his diet, and the appetite had been good. During the last month it had been

¹ American Journal of the Medical Sciences, August, 1900.

excessive, and there had been also marked thirst. Immediately after eating the food would seem like a weight in the stomach, and there would arise a sense of exhaustion, lasting for a few minutes, or even for a half-hour. More or less belching of gas would occur, a rumbling in the abdomen was frequently to be heard, and peristalsis in the epigastrium was occasionally to be seen. Of late he had had nausea at times, although vomiting was rare. The bowels were constipated, but the dejections were not unnatural in appearance.

In the last week or two there had been attacks of palpitation, sometimes relieved by the expulsion of gas. During the same period he had felt faint and had looked pale for a while two or three times daily, and had suffered more or less from dull pain in the temples. He had no cough, but was somewhat short-breathed on ascending an elevation. His breath at times smelled queerly.

During the last month he had been obliged to micturate six or seven times during the night, and then passed over two quarts of urine, although not more than a pint in the daytime. There was nothing abnormal in the appearance of this secretion. The skin had been dry throughout the illness, although during the summer months he would sweat at night. He gained five or ten pounds in weight, but had lost so much strength that he had ceased work on this account. His legs easily tire, but his feet did not swell.

On physical examination the face was pale; temperature, 99° F.; pulse, 88; respirations, 20. The heart and lungs were negative, with the exception of the presence of a systolic murmur at the base and apex of the heart. The urine was 1044, alkaline, with a slight trace of albumin, but no sugar. The examination of the blood showed 4,912,000 red corpuscles, 10,000 leucocytes, and 70 per cent. of hæmoglobin.

The epigastrium and left hypochondrium were swollen and tense from the presence of a rounded resistant tumor extending downward and backward to the vicinity of the left twelfth dorsal vertebra, thence forward three finger-breadths above the crest of the ilium toward the median line. The upper border as determined by dulness on percussion was as high as the left nipple. The lower border formed a sharply defined rounded surface. The tumor was elastic, of doubtful mobility, and presented a rounded prominence from the upper just below the left lower costal cartilage in the mammillary line. A wave was to be recognized in the left portion of the tumor. The position of the mass behind the stomach was indicated by the overlying tympany in the upper epigastrium, with easy upward displacement of the gas, and by the ready production of a splashing sound in front of the upper portion of the tumor.

Fitz made the diagnosis of cyst of the pancreas, and the subsequent operation undertaken by M. H. Richardson fully verified the diagnosis. Histologically the tumor proved to be essentially a multilocular cystoma.

Lesions of the Pancreas Simulating Gallstone Impactions. M. H. Richardson¹ has been struck by the frequent occurrence of pancreatic tumors discovered during explorations for suspected gallstones. In most of these cases the nature of the tumor has been sufficiently obvious; the history has strongly suggested cancer of the pancreas, and the exploration has removed the last doubt. But in some a doubt has always remained whether after all the tumor, which certainly caused the symptoms, was really malignant or not. Richardson then reports a case in which at the operation a tumor of the head of the pancreas was found and believed to be a cancer. The course of the disease, however, showed that it must have been some benign transitory swelling, for the patient entirely recovered. Richardson remarks that the pancreas, being so deeply situated, may be, for all that we know, especially liable to mild affections attended by actual changes in size and consistency which we may never even suspect.

Such a possibility has seemed not unreasonable, in view of the frequent observations made upon the living during exploratory operations for obscure conditions in the region of the biliary tract. From the evidence of post-mortem examinations only it must be concluded that changes in the pancreas causing stenosis of the common duct are usually malignant and beyond aid. Assuming the frequent occurrence of the mild and temporary changes in the pancreas, however, and remarking the absence of such changes upon the autopsy-table, it must be concluded that these mild changes are usually self-limited and curable, and that they have little importance in the discussion of surgical questions connected with the pancreas, except as a possible explanation of those attacks of transitory jaundice upon which a mistaken diagnosis of gallstones is occasionally based.

It is, however, with those chronic pancreatic enlargements, which threaten life by encroaching upon and closing the common duct, that surgeons are chiefly interested. Are there lesions which closely simulate cancer and which, unrelieved, will cause death, but which by so simple an operation as cholecystotomy may be cured? May we hope by surgical measures to effect a cure either by removing the disease itself or by counteracting its effects? It must be admitted that the pancreas is the seat of lesions which resemble cancer so closely that discrimination is impossible, even when the gland is palpated between the fingers.

¹ Philadelphia Medical Journal, October 6, 1900.

Richardson gives the following important points with regard to diagnosis and treatment of these conditions :

In the diagnosis between a gallstone impaction and cancer of the pancreas, ascites with jaundice favors cancer. Gradual loss of weight and the absence of pain are strong confirmatory signs.

A persistent jaundice not owing to gallstones requires a thorough investigation of the course of the common duct through the pancreas. When that exploration shows the cause to be cancer, the operation must be abandoned or limited to palliation.

If the obstruction is in the duodenal papilla, it may be remedied by operation through the duodenum. When the obstruction is probably caused by diffused hypertrophy of the gland, probably a chronic inflammation, drainage of the gall-bladder is indicated ; when to a benign neoplasm, a calculus, the contraction of cicatricial tissue, the operator must, after exact demonstration of the mechanical cause, either attempt its removal or provide a new channel for bile by means of a cholecystenterostomy.

Experimental Pancreatitis. Simon Flexner,¹ who has done a great deal of good work on the pancreas, has just published a series of experiments on animals bearing upon the question of pancreatitis and fat-necrosis. Flexner has injected acids, alkalies, bacteria, etc., into the pancreas, and studied the results. He was led to the conviction that (1) hemorrhage, *per se*, is a common condition in all forms of pancreatitis ; (2) when it is excessive it dominates the process ; (3) it is usually more pronounced than the inflammatory lesions, and the two conditions may be separate and distinct in the same organ or parts of the organ ; (4) fat-necrosis is due to perversion of the pancreatic secretion and the direct result of the action of the fat-splitting ferment. Owing to the severity of the means used to provoke pancreatitis in experimental cases, it is not to be supposed that hemorrhage would commonly occur independently of inflammation of the gland ; and this is found to be the case. It will be recalled that Flexner described the disintegration of the pancreatic tissue as being one of the results of free hemorrhage. If we now recall the tendency of the pancreatic secretion to act upon the pancreas, as has been pointed out by several writers, it follows that these injured foci might easily become the starting-points of another form of degeneration which would lead to necrosis of the gland and to reactive inflammation ; that this dead tissue might then in turn form a favorable point for the location and multiplication of micro-organisms, whose presence would still further complicate the process.

¹ University Medical Magazine, January, 1901.

Diseases of the Pancreas and Fat-necrosis Due to Obstruction of the Pancreatic Duct by a Biliary Calculus. Opie¹ has investigated the relations of pancreatic disease and cholelithiasis. The common bile-duct and the main duct of the pancreas unite in the diverticulum of Vater before reaching the lumen of the duodenum. It appears quite natural that changes occurring in one may produce pathological conditions in the other. While jaundice is due to retained products of bile secretion, according to Opie, fat-necrosis is caused by occlusion of the pancreatic duct and penetration of the secretion into the surrounding tissue.

In a series of experiments Opie has shown that ligation of both pancreatic ducts in the cat causes very wide-spread fat-necrosis, involving almost the entire abdominal fat, at times the subcutaneous and pericardial fat, and reproduces the wide distribution occasionally observed in human beings and in animals. If the ducts are ligated and pilocarpine is subsequently administered to the animal in order to stimulate the secretion of the pancreas, the dissemination of the pancreatic secretion is much hastened, and very wide-spread focal fat-necrosis rapidly occurs. The experiments show that when the outflow of the pancreatic juice is obstructed the products of secretion, dammed back upon the gland, penetrate into the tissue surrounding it and produce alterations which serve as an indication of their presence. The pancreatic lesions which in human cases are associated with necrosis of fat are such as permit the penetration of the secretion into the tissue.

Fat-necrosis may be regarded as an index of pancreatic disease, and is, therefore, an important factor in the study of lesions affecting the organ. The condition is a consequence of pancreatic lesions much as jaundice is a symptom of hepatic disease, and is not, therefore, an independent morbid entity.

Opie then describes a case in which lesions of the pancreas were associated with the impaction of a stone near the orifice of the common duct. The case is as follows :

L. F., male, aged forty-seven years. The patient was admitted to the Johns Hopkins Hospital, service of Dr. Osler, complaining of abdominal pain and fever. His family history was unimportant. With the exception of rather frequent attacks of indigestion, characterized by pain after eating, distention, and rarely nausea and vomiting, he had enjoyed good health. He did not use alcohol in any form. Six months before his present illness he suffered from an attack of jaundice, lasting about three weeks, and accompanied by abdominal pain and some fever. His stools at this time were somewhat clay-colored. At the end of three weeks he felt perfectly well.

¹ American Journal of the Medical Sciences, January, 1901.

The present illness began eighteen days before admission to the hospital, when about 9 P.M. the patient was suddenly seized with violent nausea and vomiting, accompanied by intense cramp-like pain in the abdomen. The vomiting continued during the first night, and had since only occasionally recurred. The abdominal pain, which was not localized, remained severe during four or five days, and at times there were symptoms of collapse. The abdomen was distended and the bowels were constipated until the fifth day, when, with the aid of a purgative, a movement occurred. The stool was normal in color. On the third day elevation of temperature to 101.5° F. was noted. About the seventh day tenderness and slight swelling were noticed in the right hypochondriac region. Since that time the patient had an irregular temperature (100° to 103° F.), with several chills; the pulse, 100 to 120 a minute, had been at times dicrotic. After the first few days the abdominal pain and tenderness had not been severe, but distention of the abdomen had gradually increased. Jaundice had not been noted.

Physical Examination (note by Dr. Fletcher). The patient was a large-framed man. The complexion was somewhat sallow and the conjunctivæ had a slightly yellow cast. The pulse was of fairly good volume, regular in force and rhythm. Examination of the heart and lungs was negative. On inspection of the abdomen the right costal groove was found to be partly obliterated. A distinct prominence occupied the right hypochondriac and right half of the epigastric region, and extended into the upper half of the umbilical region. Its lower margin, which descended on inspiration, was felt in the median line at the level of the umbilicus; in the mammary line, 10.5 cm. below the costal margin. Its right border could not be sharply defined. In the median line the fingers could be pressed in above it. Over the resistant mass there was dull tympany, continuous with the hepatic flatness. Leucocytes, 18,300. Urine, clear; specific gravity, 1017; acid. There was no reduction of Fehling's solution. A trace of albumin was present.

On the second day after admission a stool passed was of golden-yellow color. On the third day the leucocytes numbered 19,500, and the temperature varied from 99.2° to 101.8° F. During the night the patient was irrational at times. The temperature rose gradually, reaching a maximum of 104° F. A liquid stool of ochre-yellow color was passed. Urine: specific gravity, 1020; no reaction for sugar was obtained.

The diagnosis of suppurative pancreatitis was made by Dr. Bloodgood, and an operation for its relief was performed under cocaine anæsthesia. A linear longitudinal incision was made below the costal margin within the right mammillary line. After incising the great omentum

between the stomach and transverse colon an abscess cavity was entered. Grumous purulent fluid containing necrotic particles was evacuated. A rubber drainage-tube, packed about with gauze, was inserted into the wound. After operation the pulse remained weak, and death followed at the end of about four hours. The duration of the fatal illness was twenty-one days.

The autopsy revealed the following: Cholelithiasis; calculus lodged in the common duct near its orifice; slight jaundice. Old hemorrhage within and about the pancreas; localized necrosis of pancreas; chronic interstitial pancreatitis; necrosis of fat of pancreas, greater and lesser omentum, mesentery, and subperitoneal tissue of abdominal wall. Peripancreatic abscess limited by lesser peritoneal cavity.

Opie concludes that where anatomical conditions are favorable disease of the pancreas may occur as a complication of cholelithiasis when a calculus passes along the common bile-duct. The lodgement of a stone near the orifice of the bile-duct, where it may at the same time compress and occlude the duct of Wirsung, is not uncommonly a cause of pancreatic lesions and disseminated fat necrosis. Should a calculus become impacted in this position the preceding cases have shown that one of several, conditions may result:

1. An individual, usually in fairly good health, with perhaps a history of previous gallstone colic, is suddenly attacked with pain in the epigastric region, accompanied by vomiting and followed by collapse. Death follows usually within forty-eight hours, and at autopsy gallstones are found in the bile passages, while that one which caused the fatal attack may be still lodged in the common duct near its orifice. The pancreas is enlarged, infiltrated with blood, and hemorrhages may have occurred into the surrounding tissue. Foci of fat necrosis are usually present.

2. A fatal termination may not follow rapidly the symptoms mentioned. Pain in the epigastrium persists, jaundice may be present, and a tumor mass above the umbilicus may indicate a probable lesion of the pancreas. At the end of one or more weeks or months death occurs, often with symptoms indicating the presence of suppurative inflammation, presumably in the neighborhood of the gland. At autopsy the diagnosis of cholelithiasis is confirmed by the presence of gallstones in the gall-bladder or in the bile-ducts, and occasionally the offending calculus is still lodged near the junction of the common bile-duct and the duct of Wirsung. The pancreas is dry, black, and necrotic, and evidence of previous hemorrhage may be present. Secondary infection has occurred and the pancreas lies in an abscess cavity formed by the bursa omentalis. In the wall, and often widely disseminated in the abdominal fat, are foci of necrosis. Since the individual has survived

the primary lesion opportunity has been given for the development of secondary changes in the injured pancreas and neighboring fat.

3. In certain instances long-continued or repeated obstruction of the pancreatic duct by gallstones does not cause the acute lesions described, but produces chronic inflammatory changes.

Cancer of the Pancreas. Staples¹ reports a case of carcinoma of the pancreas, and in connection with it discusses this affection at length. As regards diagnosis, a tumor is discoverable in less than one-half the cases. There are usually symptoms of obstruction of the bile and pancreatic ducts. Undigested meat fibres are observed after a meat diet. Fatty stools are not characteristic, as is often stated.

In cancer of the colon there are usually symptoms of intestinal obstruction, a movable tumor, and occasionally intestinal hemorrhage. In great emaciation it may resemble abdominal aneurism. The pulsation is distensive in this; in pancreatic cancer the movement is up and down.

Villar says the principal physical sign of a pancreatic neoplasm is a zone of dulness bounded above by the stomach resonance and below by the colon.

The treatment of pancreatic cancer is, of course, palliative; food in small quantities, frequently administered and easily digestible, or predigested. Modified milk, soups, and the various beef extracts and eggs are of value. Fats and carbohydrates should be limited. Theoretically, minced pancreas and pancreatin would be of assistance. The surgery is *nil*. The head is too closely involved in important vessels to be removed, unless the operator is willing to perform his work partially or complete it post-mortem. The tail has been successfully removed—that is, the patient has survived the operation. In cancer the whole disease is not removed, and the ultimate results are not beneficial.

THE SPLEEN.

Primary Splenomegaly. David Bovaird, Jr.,² describes two cases of splenomegaly in children. While formerly these cases have been enumerated under the head of pseudoleukæmia splenica, Bovaird considers them as a separate disease. He maintains:

1. That the affection first described by Gaucher as primary splenomegaly, or primary epithelioma of the spleen, is a definite and distinct disease.

2. That the process is not a new growth, but an endothelial hyper-

¹ Northwestern Lancet, April 15, 1901.

² American Journal of the Medical Sciences, October, 1900.

plasia of the spleen, and that it may be associated with like changes in the retroperitoneal and mesenteric lymph nodes and the connective tissue of the liver.

The symptomatology of the affection as derived from Gaucher's thesis and Bovaird's cases may be briefly summarized thus :

1. Enlargement of the spleen, beginning in childhood (second to seventh year), slow, progressive.

2. Enlargement of the liver, secondary to that of the spleen, may be considerable, but never reaches the extent of the splenic affection.

3. Simple anæmia. The only changes observed in the blood are those associated with any chronic enlargement of the spleen.

4. Softening of the gums with oozing of blood.

5. Epistaxis repeated. Osler has noted the association of this symptom with chronic splenic enlargements.

6. Cutaneous hemorrhages and icterus, present in Gaucher's case, not in Bovaird's.

7. Symptoms referable to the mechanical effect of the splenic enlargement: pain in the abdomen; disturbance of functions of stomach and bowels; dyspnœa; dysuria; cramps in the legs.

8. The case recorded by Picou and Raymond shows that the earlier stages of the disease may be overlooked and the first evidence of the enlargement of the spleen be the effect of its weight.

9. The problem of the clinical differentiation of cases of the type herein reported from splenic anæmia must be left to the experience of the future.

N. E. Brill¹ describes three cases of primary splenomegaly occurring in one family. Brill believes that we have to deal with a family disease whose essential characteristics is a progressive splenomegaly.

¹ American Journal of the Medical Sciences, April, 1901.

GENITO-URINARY DISEASES.

By WILLIAM T. BELFIELD, M.D.

INFECTIONS.

Gonorrhœa. The literature of gonorrhœa for the year presents but little that is novel or important in either pathology or treatment. There is apparent a more general recognition of the necessity for all available diagnostic means, including staining and cultures, in order to discriminate between the gonococcus infection and those others whose most prominent early symptom is a purulent discharge from the urethra. This was emphasized by Cabot and Fuller in a discussion following the report by the former of a case in which, three weeks after coitus, a profusely purulent urethritis began; the pus contained diplococci morphologically identical with gonococci, decolorized by Gram's method, but not growing on meat serum agar. Cabot did not consider them gonococci; he believed the patient's gouty condition responsible for such modification of the urethral tissues as to render them a suitable soil for the growth of the diplococci, which may have been derived from sources other than intercourse. Fuller suggested that this source might have been an old infected focus in the prostate, and joined in the admonition to use all possible measures for differential diagnosis in doubtful cases.

EXTRA-GENITAL INFECTION. Kars¹ reports two cases of rectal gonorrhœa following the evacuation of a prostatic gonorrhœal abscess into the rectum—one spontaneous, the other by incision.

Colombini² describes a stomatitis gonorrhœica in a prostitute, cured in eight days by treatment with potassium permanganate solution, 1 to 1000, and silver nitrate, 1 to 20.

GONORRHŒA A BLOOD INFECTION. Cases of blood infection by the gonococcus, identified by cultures, become more numerous with the more general adaptation of this method of accurate diagnosis. The proof of secondary local infections by the gonococcus (and incidentally of transfer of this bacterium by the blood current) began in 1892, when Lindeman³ obtained pure cultures of it from gonorrhœal arthritis; similar proof as to the gonococcus infection of tendon-sheaths was furnished in

¹ Berliner klin. Wochenschrift, 1901, No. 4.

² Riforma Med., 1900, No. 87.

³ Beiträge zur Augenheilk., 1892, p. 32.

1893 by Tollemer;¹ of the perichondrium, in 1894, by Ghon and Schlagenhauser;² of the pleura, by Mazza; of the blood and the endocardium, by Thayer and Blumer,³ in 1895; of the cervical glands, in 1896, by Pettit and Pichevin;⁴ of the parotid gland, by Colombini, in 1897;⁵ and of the pericardial exudate, by Thayer and Lazear,⁶ in 1898.

The literature of the past year contains reports of fatal gonococcus infection of the endocardium by McCaskey,⁷ Lartigau,⁸ Wassermann,⁹ and Neisser.¹⁰

That the gonococcus can infect the urinary as well as the genital organs and the subjacent peritoneum has been repeatedly demonstrated since it was first proven by Wertheim. Young¹¹ observed a cystitis of five years' duration following gonorrhœa, with double pyonephrosis; the urine obtained by suprapubic aspiration gave a pure culture of the gonococcus—indicating that this parasite may cause a chronic as well as an acute bladder infection. Lewis¹² describes the post-mortem findings in a case of fatal acute nephritis caused by gonococci. Prochaska¹³ obtained from the blood in two cases of gonorrhœal arthritis typical growths of the gonococcus on ascites agar and ascites bouillon.

Heller¹⁴ describes a case of unmixed gonococcus infection of the bladder; the cystitis was accompanied with hemorrhage. A gonorrhœal ulcer was discovered in the bladder, and finally curetted, curing the cystitis. Doléris¹⁵ reports a case of gonorrhœal cystopyelitis, pericarditis, and renal abscesses; gonococci were found in the blood and pericardial exudate.

Batal¹⁶ describes gonorrhœal disease of the knee and elbow-joint, an osteoma appearing in the latter.

Hirtz¹⁷ observed large hypertrophy of the diaphysis of right femur follow gonorrhœal infection of the bone. Ullmann¹⁸ had a patient who, in the third week of gonorrhœa, developed chills, fever, pain, and swelling in both elbow-joints. The left elbow was opened and drained;

¹ *Revue de Médecine*. November, 1893.

² *Archiv f. Dermatologie u. Syph.*, 1894, p. 330.

³ *Arch. d. méd. expérimentale*, November, 1895.

⁴ *Journal des maladies cutan. et syph.*, 1896.

⁵ *Centralblatt f. Bakteriologie*, Band xxiv., No. 25.

⁶ *Journal of Experimental Medicine*, January, 1899.

⁷ *New York Medical Record*, 1900, No. 52.

⁸ *American Journal of the Medical Sciences*, 1901, No. 1.

⁹ *Münchener med. Wochenschrift*, 1901, No. 8.

¹⁰ *Berliner klin. Wochenschrift*, 1901, No. 9.

¹¹ *Johns Hopkins Hospital Reports*, vol. ix.

¹² *Journal of Cutaneous and Genito-Urinary Diseases*, 1900, p. 395.

¹³ *Virchow's Archiv*, vol. clxiv.

¹⁴ *Archiv f. Dermatologie u. Syph.*, 1901, Band lvi.

¹⁵ *Presse Méd.*, July 11, 1900.

¹⁶ *Journal des maladies cutan. et syph.*, 1900.

¹⁷ *Presse Médicale*, 1900, No. 5.

¹⁸ *Wiener med. Presse*, 1900, No. 49.

on the ninth day the lower end of the humerus was chiselled open in several places, giving vent to much pus, in which gonococci and no other bacteria were found. Muscatello¹ reports acute peritonitis following an operation for pyosalpinx; gonococci, identified by cultures, were found in the pus from the tube and in the peritoneal exudate.

Ullmann² reports five cases of fatal septicæmia whose origin remained undiscovered until autopsy revealed gonorrhœal infection and a prostatic abscess in each. He adds an exhaustive review of the literature of general infection and metastases from gonorrhœa.

Eulenburg³ discusses the disturbances of the nervous system caused by gonorrhœal infection. He recognizes: 1, neuralgia, especially lumbar and ischiatic; 2, muscle atrophy and paralysis; 3, neuritis and myositis; 4, disease of the spinal cord simulating tabes, but attacking the motor sphere more distinctly.

Christmas⁴ reports a series of interesting observations on the effects of gonococcus toxins when introduced into animals by intracerebral and subcutaneous injection. He finds that a poisonous dose immunizes, so that the animal endures one hundred times as much subsequently; also that the subcutaneous injection causes the generation of an antitoxin which neutralizes the poison, and that this antitoxin gives immunity to a second animal, which immunity vanishes, however, after three days. Hanislawsky⁵ reports another case in which during an acute gonorrhœa the patient developed an arthritis involving the feet and right knee, and an exanthem of horny efflorescences, loss of nails on both feet, and red patches in the mouth—all suggesting syphilis, but not affected by mercury and iodine. After some weeks the discharge ceased, and all these symptoms disappeared; later the patient returned with renewal of the discharge and of the exanthem.

Paulsen⁶ observed a case of ophthalmia gonorrhœica neonatorum in which, on the tenth day after birth, there developed an arthritis of each knee. The left knee was incised, the evacuated pus containing gonococci. Soon after the arthritis began there occurred on the face and extremities an eruption of papules and vesicles, the fluid of the latter containing gonococci.

In this connection the observation of Heller⁷ is of interest, according to which urethral injections of 20 per cent. creolin solution were followed by a purulent discharge and by multiform erythema.

¹ Centralblatt f. Krankh. der Harn. und Sex. Org., 1900, p. 673.

² Deutsch. Archiv f. klin. Med. 1901, p. 309.

³ Centralblatt f. Krankh. der Harn. und Sex. Org., 1900, p. 677.

⁴ Annales de l'Institut Pasteur, 1900, p. 331.

⁵ Monatsb. auf dem Gebiete der Harn. und Sex. Org., Band v. p. 88.

⁶ Münchener med. Wochenschrift, 1900, No. 35.

⁷ Deutsch. med. Wochenschrift, March 14, 1901.

TREATMENT. The long-sought antidote to the gonococcus infection, which, taken into the blood, shall reach all the follicles and pockets of the urethra, remains to be discovered. Hence the mitigating local treatment by injections is still the chief reliance.

The potassium permanganate method is steadily falling into deserved oblivion; the compounds of silver with albumin are steadily gaining favor as local applications. Protargol remains the favorite, though a newer preparation—nargol—has decided advantages which are securing recognition; it can be injected in the acute stage combined with berberine, as follows:

Berberine (yellow hydrastin) muriate	1 grain.
Nargol (or protargol)	5 grains.
Water	1 ounce.

injected four to six times daily and retained two or three minutes each time. The percentage of nargol or protargol is increased as the inflammation subsides. After the first week, when the infection has invaded the deep urethra, the injection must be made to follow it. This is accomplished by having the patient inject with a syringe holding at least an ounce, and relaxing the cut-off muscle during the injecting process.

GONORRHOEAL ARTHRITIS. Leistikow¹ reports fourteen cases of acute gonorrhœal arthritis as recovering completely in three to five weeks, under the following treatment, in addition to treatment of the urethral infection: 10 per cent. ichthyol-vasogen was rubbed several times daily into the infected parts, which were then bandaged with gutta-percha or oiled silk and cotton. Internally three to five drops of ichthyol were given, with plenty of water, after each meal.

RELATION OF CHRONIC GONORRHOEA TO STERILITY. The usual view that the prostatic secretion in chronic gonorrhœa of the prostate is always alkaline is contested by Lohnstein² on the basis of 540 examinations of such fluid. He found the reaction to be alkaline in 20 per cent., neutral in 5 per cent., acid in 70 per cent. Of eighty-two cases with alkaline secretion there were found in fifty-six moving, in twenty-six motionless, spermatozoa.

He concludes that an alkaline prostatic secretion does not necessarily impair motility of spermatozoa nor cause sterility.

In the discussion Posner remarked that motility and fertilizing power of spermatozoa are not in constant ratio; and Casper argued that since chronic prostatitis occurs in 80 per cent. of chronic gonorrhœa, it does not often cause sterility.

¹ Monatshefte f. prakt. Dermatol., 1900, No. 31.

² Berliner Verein f. inner. Med., October 15, 1900.

Kehrer¹ says that azoöspemia frequently follows long-continued gonorrhœa, even when only one testicle is invaded by the infection. He observed azoöspemia in a man, one of whose testicles had been removed because of gonorrhœal inflammation and hydrocele, the remaining organ never having been diseased. The patient's wife admitted that her two children had been begotten by another man.

Kehrer suggests the wisdom of examining the semen in every case of protracted gonorrhœal infection.

There is no doubt that the systematic examination of semen would add greatly to our knowledge of the extent and the causes of sterility in the male. I have for years had under my observation a healthy man who was formerly the subject of protracted gonorrhœal infection of the prostate and both vesicles, without acute epididymitis, whose semen, nevertheless, contains no spermatozoa whatever. I recall an instance, similar to Kehrer's, of a man whose wife, after six years of sterile marriage, became pregnant under circumstances which aroused the husband's suspicion of her fidelity. He admitted a chronic gonorrhœa with unilateral epididymitis prior to marriage, but asserted that the second testicle had always been free from disease; yet his semen contained no spermatozoa. Confronted with these facts, the wife confessed adultery.

Tuberculosis. Infection of the genito-urinary organs is now generally recognized as extremely frequent in males between fifteen and thirty years of age—so frequent, indeed, as to be second only to the gonococcus infection in point of numbers. This infection constitutes, therefore, an important factor in the work of the genito-urinary surgeon; and while the recognition of it presents usually but few difficulties to modern diagnostic methods, the successful treatment is still dubious in any given case. Individual instances of the apparent healing of undoubted tuberculosis, sometimes extensive, of the genital or even of the urinary tract by medicinal and hygienic measures are numerous; while the failure of all such, even when reinforced by surgical aid, is by no means infrequent.

One of the chief questions still under discussion concerns the proper limitations of surgical interference. The original idea, that excision of a tuberculous focus usually removed the infection, has been rather thoroughly eradicated by clinical experience, which, indeed, has merely corroborated the earlier teaching of the necropsy-table that the tuberculous infection is—at least when it reaches the surgeon—commonly multiple; that the focus discovered and removed was but one of several, and especially that more formidable, from the therapeutic stand-point

¹ Münchener med. Wochenschrift, 1900, No. 36.

than one or two tuberculous foci, is the underlying tissue defect which constitutes susceptibility to the infection. On the other hand, experience has shown that the removal of an extensive tuberculous deposit and consequent decrease in the amount of toxins circulating in the blood may, combined with appropriate medicinal measures, be followed by partial or complete arrest of activity in the remaining foci, even when numerous. This beneficial effect has been especially noted after the removal of a tuberculous kidney or epididymis.

A review of the year's literature on the treatment of genito-urinary tuberculosis is, therefore, a record of conflicting experiences and of diverse opinions.

The Genito-Urinary Section of the Thirteenth International Medical Congress, at Paris, devoted much time to an elaborate and exhaustive discussion of tuberculosis of the urinary organs. The consensus of opinion was: 1, that local medical treatment is rarely successful; 2, that surgical attempts at mitigation—including curettement of the tuberculous bladder, resection of the kidney, nephrotomy—are seldom beneficial, but often harmful; 3, that bladder tuberculosis is regularly secondary to some prior localization of the infection; 4, that renal tuberculosis is often primary; 5, that nephrectomy is the only proper surgical treatment for renal tuberculosis, as well as the only operation for tuberculosis anywhere in the urinary tract, which gives satisfactory results.

The mortality of this operation has been in recent years reduced to 12 and even to 9 per cent.; the fatal results are usually attributable to extensive infection of the opposite kidney. The functional activity of this latter organ has been in many cases ascertained before operation by catheterization of the ureter, and in the past year by combining with this measure the use of phloridzin. Casper narrated such a case, in which the failure of a kidney to excrete sugar after phloridzin was administered averted an operation on the opposite (tuberculous) kidney.

Motz called attention to the fact that urinary tuberculosis is occasionally healed by the unassisted vital forces; he asserted that he had seen four such instances of spontaneous healing of bladder tuberculosis, and three of the same infection in the kidney.

Pousson presented a collection of 600 cases of surgical intervention in renal tuberculosis, many of which, however, antedated the period of exact diagnosis as now practised. Nephrectomy gave excellent, nephrotomy poor, results.

Albarran stated that his personal experience comprised twenty-nine nephrectomies with one death, fifteen nephrotomies with one death. He advised early nephrectomy, even if the other kidney be slightly diseased.

Motz reported recovery in fourteen out of sixteen nephrectomies, many of them apparently permanently cured.

Simon¹ reviews the surgical treatment of renal tuberculosis in thirty-five patients—twenty-five women, ten men. In only two was there genital tuberculosis also—once in the vulva, once in the testicle. Tubercle bacilli were found in the urine in only ten cases; in three cases the diagnosis was made by means of tuberculin, in eleven by the cystoscope, in three by the ureteral catheter, in the remaining eight by symptoms.

The remote results of nephrectomy were far better than those of nephrotomy; the former operation gave nearly 50 per cent. of permanent cures.

Israel² has operated thirty-one subjects of renal tuberculosis, performing nephrectomy twenty-eight times and nephrotomy three times.

Of the nephrectomies three died immediately (11 per cent.), and five others in periods from three weeks to eight months after operation, of various tuberculous lesions. Ten cases have enjoyed excellent health and are apparently cured. He remarks upon the frequency with which renal tuberculosis is primary, stating that in eighteen of his operated cases the infection was primary in the kidney, in three secondary, and in five doubtful. He strongly advocates nephrectomy.

Koranyi³ relates two instances in which the injection of tuberculin transformed a mere suspicion of renal tuberculosis into a positive diagnosis. In one case the urine presented no abnormality, but the right kidney reacted to the injection. The kidney was removed and the diagnosis confirmed. In the second case both kidneys reacted, and operation was for that reason omitted.

Richter⁴ saw a case of vesical tuberculosis symptomatically cured by the internal administration of ichthyol after various other treatments had failed.

Ehrmann⁵ observed six cases of tuberculous ulcer (bacilli demonstrated) at or near the meatus in patients elsewhere tuberculous; also a tuberculous ulcer on the greater labium of a fifty-six-year-old woman who presented no other discoverable tuberculous lesions. Blondini⁶ infers from experiments on animals that tubercle bacilli may wander from the meatus to the testicle along the mucous surface; congestion of a part (as in puberty) favors the growth of these bacilli.

¹ Beiträge zur klin. Chir., 1901, Band xxx.

² Klinik der Nierenkrankheiten, Berlin, Hirschwald, 1901.

³ Centralblatt f. Krankh. der Harn. und Sex. Org., 1900, p. 483.

⁴ Deutsch. med. Zeitung, 1900, No. 22.

⁵ Wiener med. Presse, 1901, No. 5.

⁶ Annales des Mal. des Org. Gen.-Urin., October, 1900.

Baumgarten,¹ on the other hand, asserts as the result of much experimental and anatomical research that tubercle bacilli are never carried against the blood, lymph, and secretion streams—*i. e.*, never from prostate and bladder to kidney, and never from prostate to epididymis.

GENITAL TUBERCULOSIS. The proper limitation of operative interference in tuberculous disease of the genital organs in the male continues to be the subject of discussion. In favor of radical measures is the contention that while most cases when they reach the surgeon have multiple foci of infection, some of them undiscoverable, and some inaccessible, yet the removal of all tuberculous tissue accessible to the knife lightens the intoxication and often enables the organism to overcome the remaining foci. The advocates of conservatism, on the other hand, maintain that curetting and resection—of the epididymis, for example—accomplish all that can be expected of castration, without sacrificing the valuable internal secretion of the testicle or draining the patient's vitality by the shock of the more serious operation; and this contention is supported by the best clinical results.

Bruns² favors castration for tuberculosis of epididymis and testicle; in his own observation unilateral castration has cured 46 per cent. of cases, bilateral 56 per cent., observation having extended from three to thirty years after operation.

This subject was exhaustively discussed in the last meeting of the Congress of German Surgeons, held in Berlin in April, 1901.³ Bruns was followed by Simon, who summarized the experience of the Heidelberg clinic for twenty-seven years past, as follows: 107 patients had undergone single or double castration for tuberculosis of the testicle or epididymis, and the subsequent history of 92 of these was known: 33 died (26 of tuberculous lesions); in 26 of the living there was a distinct retrogression of distant tuberculosis, especially of the lungs. Double castration was performed thirty-four times, and the subsequent history was known in 29 cases; 8 died of various tuberculous lesions, 21 still live. Secondary removal of the second testicle (performed in 15 cases) was repeatedly followed by remarkable improvement in the general condition, and by retrogression of the infection in the prostate and bladder.

In only 1 case was double castration followed by psychic disturbances; 5 showed decrease in sexual desire; while in all others there occurred not the least impairment in sexual desire or power, even when the observation had lasted twenty years after castration.

Of the 92 cases, 54 still live; 7 others, after years of freedom from

¹ Archiv f. klin. Chirurgie, Band liii. p. 1010.

² Ibid., p. 1014.

³ Centralblatt f. Chirurgie, 1901, No. 29. Beilage.

tuberculosis, died of other diseases ; hence, Simon considers 61 cured (66 per cent.)—certainly a remarkably high ratio.

König expressed his reluctance to castrate because the infection has usually involved the prostate and vesicles, and commonly progresses after castration.

Gussenbauer stated that he performs castration only when the disease is very extensive in the testicle, preferring excision and curetting of the tuberculous foci in other cases. Henle, Bier, and Schlange were averse to double castration.

Longuet,¹ after an elaborate discussion of the subject, concludes : 1, that castration is an error ; 2, that conservatism carried to complete abstention from operative measures is equally erroneous ; 3, that conservative operation is the wise course.

Mauclair finds that ligation and section of the spermatic cord, excluding the artery, whereby gradual atrophy of the testicle is induced, is a valuable measure for arresting tuberculosis, provided no suppuration or fistula pre-exists.

Young presented to the annual meeting of the American Association of Genito-Urinary Surgeons an admirable thesis² on genital tuberculosis, based on extensive personal experience and acquaintance with the literature. He is convinced :

1. That in the early stage the infection is usually confined to the epididymis, the testicle being rarely involved.

2. The testicle is of value, even though its duct be occluded.

3. Epididymectomy is as effective and as free from recurrence as is castration.

4. After either operation, the opposite organ is often found to be infected ; and as double epididymectomy is less harmful than double castration, epididymectomy is preferable to castration.

5. Epididymectomy with high resection of the cord is the operation of choice.

6. Castration should be limited to cases where the testicle is involved or scrotal infection is extensive.

7. Double castration should be avoided.

8. Operations upon the seminal vesicles and prostate should be undertaken only after removal of testicular foci has failed to arrest the disease and it has spread to the bladder. Serious involvement of distant parts—pulmonary, urinary, osseous—does not contraindicate operation, especially if cocaine be used as the anæsthetic.

9. That remarkable disappearance of extensive tuberculosis of pros-

¹ *Revue de Chirurgie*, January, 1900.

² To be published in *Annals of Surgery*, November, 1901.

tate, seminal vesicles, bladder, kidneys, lungs, etc., may follow simple removal of the testicular foci, seems abundantly proven.

Young¹ also reports the removal of the tuberculous seminal vesicles in two patients by a new operation: he makes a median incision into the abdominal cavity, extending from the symphysis to an inch above the umbilicus; then a transverse section of the right rectus muscle an inch above the umbilicus; he opens the bladder above the symphysis and catheterizes both ureters; he then strips the peritoneum from the bladder, exposing the vesicles and vasa deferentia to the prostate. Then the vesicles and cords are excised and the wound closed with drainage. The peritoneum should be stripped from the bladder chiefly in the median section, avoiding the ureters and rendering preliminary catheterism of these ducts less essential. The vasa deferentia are more easily identified in their lower segment, near the vesicles, than above this point. Upward traction of the bladder aids in bringing the vesicles up toward the abdominal wound.

By this method Young has successfully removed not only the vesicles and vasa, but also in one case² about half of the tuberculous bladder in addition. Young's operation certainly materially reduces the difficulties inherent in all other methods for removing the seminal vesicles, and renders these organs legitimate objects of surgical attack.

König³ (Altona) reported four cases in which he had operated for tuberculosis of the prostate and vesicles by resection of the sacrum, with operative recovery.

Möller⁴ describes a case of primary tuberculosis of the prostate, developing two years after traumatic suppuration in this organ; autopsy showed secondary miliary tuberculosis of the peritoneum and abdominal organs, of the pleura, lungs, pericardium, and meninges. He refers to Oberländer's⁵ four cases of primary prostatic tuberculosis following injury, and to Kapsamer's⁶ three cases of miliary tuberculosis following cheesy nodules in that gland.

SYPHILIS. Chrzelitzen⁷ reports a case of syphilis of the bladder and testicle, and refers to fourteen cases of syphilitic cystitis previously reported.

¹ Archiv f. klin. Chirurgie, Band lxii. p. 456.

² Annals of Surgery, October, 1900.

³ Centralblatt f. Chirurgie, 1901, No. 29. Beilage.

⁴ Ibid., p. 157.

⁵ Centralblatt f. Krankh. der Harn. und Sex. Org., 1900, p. 9.

⁶ Wiener klin. Wochenschrift, 1899, p. 1029.

⁷ Centralblatt f. Krankh. der Harn. und Sex. Org., January, 1900.

PYOGENIC INFECTIONS.

Brown¹ discusses the bacterial varieties which are instrumental in the induction of cystitis, and affirms that the colon bacillus is, by virtue of its frequency, especially important.

Feltin² reviews Wreden's well-known work on bladder infections after injury to the rectum, published in 1893, and offers a long experimental series of his own which lead him to somewhat different conclusions. He finds that injury to the rectum at the level of the prostate is not, as Wreden asserted, sufficient to permit migration of colon bacilli through the rectovesical partition into the bladder; only when the rectal injury was sufficient to induce peritonitis did there occur an infection of the bladder, and then usually by way of the blood and the kidneys.

He finds that even slight injuries to the rectum may be followed by migration of the rectal bacteria in large numbers into the rectovesical tissue; and that if artificial retention of urine be associated with the rectal lesion, this migration may extend into the bladder and cystitis result.

In a later article Feltin³ relates the influence of fecal stagnation on the entrance of bacteria into the bladder and circulation. He concludes: 1, that closure of the anus (in rabbits) thirty-six to forty-eight hours does not suffice to cause flooding of the body with intestinal bacteria; that this occurs only after long occlusion of the bowel, and in the last hours of life; 2, that after prolonged fecal stagnation, intestinal bacteria can enter the bladder through the vesicorectal septum or the urethra; and that such entrance is favored by ligation of the penis so as to produce retention of urine.

Blumer and Lartigau⁴ relate three fatal cases of ascending urinary infection by the bacillus pyocyaneus and proteus vulgaris. In one the clinical picture was that of hemorrhagic septicæmia, though the bacteria were found post-mortem in the urinary organs only.

Reynes⁵ classifies the vesical complications of appendicitis as: 1, reflex influence, shown by retention or incontinence; and 2, the direct extension of the infection, causing cystitis, pericystitis, vesical hemorrhage, and calculus.

Allan⁶ relates another case of appendicular abscess bursting into the bladder, with recovery; and Keen details his troubles, diagnostic and

¹ Johns Hopkins Hospital Bulletin, January, 1901.

² Centralblatt f. Krankh. der Harn. und Sex. Org., 1901, p. 401.

³ Ibid., p. 465.

⁴ New York Medical Journal, September 22, 1900.

⁵ Revue de Chirurgie, September, 1900.

⁶ British Medical Journal, 1901, No. 17.

operative, with a case in which adhesion of a suppurating appendix to the bladder resulted in an appendiceo-vesical fistula which was finally discovered and healed by operative measures.

Albarran and Cattel,¹ in forty-three cases of suppuration in and around the urinary tract, found anaërobic bacteria with or without aërobes. The former cause the gangrenous lesions, and they may lead to general peritonitis or secondary infections elsewhere.

Guiard² called attention to the numerous cases of purulent inflammation of the genitals in the newly-married, which may even simulate gonorrhœa in intensity and yet be entirely free from the gonococcus infection. They are due to the usual vaginal saprophytes, which cause leucorrhœa and metritis even in virgins; and when their action is aided by the extreme genital congestion induced by the sexual excesses of the honeymoon, their effect may be intensified into the production of a pronounced purulent inflammation of the male as well as of the female genital canal.

Pousson³ described a case in which repeated renal hemorrhages and other symptoms led to a diagnosis of renal tuberculosis and to nephrectomy. The cut surface of the excised kidney presented nodules similar to tubercles, which were found, however, to enclose colon bacilli and no Koch's bacilli. The case is interesting also because it furnishes still another instance of unilateral septic infection, the recognition of which possibility has already resulted in several cures of such infection by nephrotomy and nephrectomy.

Karo⁴ reports two interesting cases of colon bacillus infection of the urinary tract of long standing; each patient came under Karo's observation because of the occurrence of an acute swelling of the testicle accompanied with a chill, high fever, and pain. The cloudy urine contained multitudes of colon bacilli, which were also found in the contents expressed from the prostate and vesicles. The fluctuating scrotal tumor in each case was punctured, giving vent to pus containing only the colon bacillus; in one case the evacuation of this abscess, combined with urotropin internally, was followed by recovery; in the other patient further chills and fever occurred, with suppuration in the testicle, which was finally removed.

TREATMENT. Stockmann,⁵ on the basis of experience in five cases in which he made instillations in the renal pelvis through the ureteral catheter, with good results, advises this method in the treatment of

¹ Proceedings of the Thirteenth International Medical Congress.

² Ibid.

³ Presse Médicale, 1900, No. 46.

⁴ Deutsch. med. Wochenschrift, April 11, 1901.

⁵ Wiener klin. Rundschau, 1900, Nos. 44 and 45.

pyogenic infections of the upper urinary tract ; he thinks it should be tried before resort is had to operative measures.

Pousson¹ adds four cases of acute infectious nephritis treated by nephrectomy, with two recoveries and two deaths. He has also treated three cases of chronic nephritis by the same surgical procedure ; in each case the operation was followed by a decided increase in the excretion of water, phosphates, and chlorides.

Young² describes a case of chronic infection of the bladder with the Eberth bacilli, lasting seven years after the attack of typhoid fever, and says that he has found only two other cases of chronic cystitis from the typhoid bacillus infection described in the literature. Urine obtained by suprapubic puncture gave a pure culture of the bacillus typhosus ; the urine was constantly acid. Urotropin caused a decrease, but not the total disappearance of these bacteria.

Brown³ gave each of two typhoid patients 10 grains of urotropin three times daily. On the seventh day each patient's urine contained considerable blood, which disappeared so soon as the urotropin was discontinued.

Griffith⁴ gave a convalescent typhoid patient 10 grains of urotropin three times daily ; on the tenth day there was noted general weakness, pain over the kidneys, œdema of the lids, and marked albuminuria. All these symptoms disappeared within three days after the remedy was discontinued.

CANCER.

Oberländer⁵ collects seven cases of carcinoma of the urethra in the male, being the entire number reported during the past seven years. This work corroborates the prevailing belief as to the rarity of cancer in the urethra.

Pasteau⁶ investigated at the Necker Hospital the question of the secondary infection of the pelvic lymph glands from carcinoma of the bladder. He found that these glands were cancerous in 25 per cent. of pedicled tumors, 44 per cent. of sessile, and 35 per cent. of infiltrating tumors. If clinically no evidence of such glandular involvement is found, the reason lies in the inaccessibility of these glands, the lumbar and iliac retroperitoneal lymph nodes being most frequently involved.

¹ Loc. cit.

² Johns Hopkins Hospital Reports, vol. viii. p. 401.

³ British Medical Journal, June 15, 1901.

⁴ Ibid., June 29, 1901.

⁵ Centralblatt f. Krankh. der Harn. und Sex. Org., 1900, p. 455.

⁶ Proceedings of the Thirteenth International Medical Congress.

CALCULUS.

Improvement in the technique and added experience with the Röntgen ray in the detection of calculi has revealed the greater frequency of stones lodged in the ureter than earlier clinical experience had discovered. Leonard¹ states that over half the forty-seven calculi discovered by him in the upper urinary tract by means of the X-ray have been lodged in the ureter. Moullin² agrees with Leonard that the Röntgen ray affords a trustworthy negative as well as positive diagnosis of stone in the kidney and ureter.

Schenck³ reports from Kelly's clinic three cases of operative removal of a stone from the ureter, and a fourth, operated by Halsted, is also mentioned. He states that the literature contained less than ninety such cases at the time of his report.

Keen⁴ records the operative removal of a ureteral calculus, skiagraphed by Leonard, lodged below the pelvic brim in a child ten years old.

Pozzi reported to the Thirteenth International Medical Congress a case in which a woman, who complained of menorrhagia, but never of urinary symptoms, presented a tumor in Douglas' pouch; this was incised and found to contain a calculus having the size and shape of a cigar, lying in a cyst of the ureter. The wound was sewed and healed completely.

Israel⁵ records 61 operations for nephrolithiasis, with 9 deaths (15 per cent.). Of these 29 were uncomplicated nephrolithotomy, with 1 death; 12 were for the removal of ureteral stones, with 4 deaths; 5 were nephrotomy for calculous anuria, with 2 deaths; and 15 primary nephrectomy for severely infected stone kidney, with 2 deaths.

Guyon⁶ discusses the relative merits of suprapubic cystotomy and of lithotritry for vesical calculus, referring to his experience during the last ten years at the Necker Hospital. During this period there were made 39 suprapubic lithotomies, with 11 deaths, and 555 lithotrities, with 17 deaths—a mortality of 28 and of 3.1 per cent., respectively. He shows that the extreme mortality of the cutting operation is due not to the operation but to the existing conditions, and maintains that each procedure has its permanent field.

Guyon⁷ also discusses the reasons for the recurrence of vesical stone.

¹ *Annals of Surgery*, April, 1901, and *Journal of the American Medical Association*, August 31, 1901.

² *Lancet*, January 19, 1901.

³ *Journal of the American Medical Association*, May 11, 1901.

⁴ *Ibid.*, June 10, 1901.

⁵ *Chirurgische Klinik der Nierenkrankheiten*, Berlin, 1901.

⁶ *Annales des Mal. des Org. Gen.-Urin.*, January, 1901.

⁷ *Ibid.*, May, 1901.

This follows the cutting as well as the crushing operations, and is due to the original bladder conditions. It is to be avoided by careful diet, by habitual cleansing of the bladder, and by the periodical removal (by the lithotrite) of small concretions.

Letzko¹ treated a woman suffering from ulcers of the bladder incrustated with phosphates, curetting them through the urethra twelve times in one year, with temporary improvement only. Then, through a suprapubic incision, he endeavored to remove the incrustations with a sharp spoon; failing in this he excised each ulcer and its phosphatic crust, achieving a complete recovery.

THE KIDNEY.

Congenital Cysts. Corvelaire² presents an elaborate historical, anatomical, and clinical research on this topic; he concludes that such cysts represent a fault of development.

Movable Kidney. Daubrieux,³ after a critical review of the theories as to the etiology of movable kidney, concludes that it is independent of intra-abdominal tension and obesity, and differs from enteroptosis. Harris⁴ ascribes mobility of the kidney to a disproportion between the capacities of various zones of the trunk. Trekaki said in the Thirteenth International Medical Congress that he had found a movable kidney in forty-two of one hundred Arab women taken at random, though these women never wear corset or waist-bands.

The clinically important fact is now well established that movable kidneys are often found in unmarried women, young girls, and men; hence, that pregnancy and obesity—to which the mobility was formerly ascribed—are at most merely the provocative and not the predisposing causes, which latter have yet to be satisfactorily demonstrated.

Of the operative plans for anchoring the mobile kidney, that advocated by Senn,⁵ which substitutes guy ropes for sutures to retain the organ in position during cicatrization, seems to have given the best results; the gauze ropes which Senn used are now supplanted by sterile rubber tubes, with obvious advantages, especially during their removal. It is to be noted that the fixation of a movable kidney has repeatedly arrested renal hæmaturia.

Surgical Treatment of Nephritis. The successful treatment of unilateral nephritis, subacute and chronic, and of congestive anuria by

¹ Wiener klin. Wochenschrift, 1901, No. 18.

² Annales de Gynécologie, November, 1900.

³ Société des Sciences médicales de Brux., November, 1899.

⁴ Journal of the American Medical Association, June 1, 1901.

⁵ Ibid., December 11, 1897.

nephrotomy or nephropexy, was summarized in this publication last year.¹ The present status of this therapeutic measure is well presented by Harrison,² to whom its adoption is in some measure due. He mentions six cases in his own experience in which nephrotomy, made under a mistaken or tentative diagnosis, relieved unilateral infectious nephritis.

Pousson³ removed a kidney for supposed tuberculosis, but found that the nodules contained colon bacilli. He also adds four cases of acute and three of chronic nephritis treated by nephrotomy; two of the acute cases died; all the others were cured.

Israel⁴ has operated on fourteen cases of nephritis for hemorrhage, colic, and nephralgia. He states that: 1, nephritis may be unilateral; 2, it may cause renal colic—like the obstructive form—without bleeding or other obstruction; it also causes pain radiating into the bladder and urethra; 3, unilateral nephritis may cause bilateral pain and colic; 4, severe nephritis may be accompanied by a secretion of urine permanently free from casts and albumin; or there may be found many and various casts without albumin; 5, the bleeding from nephritis may simulate malignant growths; it may occur with or without colic, which is caused not by obstruction through clots but by the renal congestion; 6, in many cases nephritis is much relieved by nephrotomy; the wound in the kidney in these cases should not be sutured.

Israel distinctly formulates in these propositions an improvement in diagnosis and treatment toward which the experience of the last few years has been steadily advancing.

Essential Renal Hæmaturia. The now generally accepted view that "essential" renal hæmaturia is the result of local renal lesions—nephritis, bacterial infection or mobility of the kidney, and renal retention—and usually requires nephrotomy, is contested by Klemperer,⁵ who still clings to the angioneurotic and hysterical hypothesis. In support of his contention he adduces several cases in which renal hæmaturia was permanently arrested by rest in bed, hydrotherapy and electricity.

Naunyn⁶ also advocates medical treatment for these cases, even when the bleeding is coincident with and apparently caused by a chronic nephritis. He mentions three cases of this disease in which profuse hemorrhage occurred repeatedly, but was always stopped without surgical interference.

¹ PROGRESSIVE MEDICINE, December, 1900, p. 77.

² British Medical Journal, August 3, 1901.

³ Presse Médicale, 1900, No. 46.

⁴ Klinik der Nierenkrankheiten, Berlin, 1901.

⁵ Therapie der Gegenwart, January, 1901.

⁶ Mittheilungen aus den Grenzgeb. der Med. und Chir., Band v. p. 639.

It is somewhat remarkable that neither of these gentlemen mentions gelatin as a hæmostatic agent—the only medicinal agent, indeed, whose record rivals that of nephrotomy in the arrest of essential renal hæmaturia. Schwabe's and my own cases were noted last year.¹ Gassner² saw a case of renal bleeding (accompanied with lumbar pain), which had long resisted various agents and methods, stop promptly and permanently after one subcutaneous injection of gelatin, 200 grammes of a 2.5 per cent. solution. Hahn,³ after futile attempts to arrest renal bleeding in a subject of hæmophilia, administered 200 to 250 grammes of gelatin daily with the food; the bleeding diminished at once and ceased completely on the third day. The patient's general health rapidly improved. These and the numerous instances in which bleeding from organs other than the kidney have been promptly arrested by gelatin corroborate the advice given a year ago⁴ that "so-called essential renal hæmaturia should be submitted to this treatment before surgical means are employed."

The effect of suprarenal extract upon essential renal hæmaturia seems still to remain unassayed.

It seems probable that cryoscopy may become, as Kümmell asserts, a reliable means for distinguishing essential renal hæmaturia due to nephritis from the other lesions that may be accompanied by renal hemorrhage, especially stone; and that the necessity and safety of nephrotomy may thus become more narrowly defined.

Renal Tumors. Israel⁵ has operated in sixty-eight cases of renal tumor, forty-five males and twenty-three females. Nephrectomy was done in forty-three cases, of which eight died of the operation; of twenty-two that have been followed three years or more, fourteen died of recurrence and eight cures have lasted from three to fourteen years. The list includes three cases of that unusual disease called malignant papilloma of the renal pelvis.

Bork⁶ collects twenty-four cases of tumor of the capsule of the kidney—fibrolipomata, myxolipomata, rarely sarcomata—twenty of these patients were women. The kidney was usually healthy, though it was removed in fifteen cases.

Anuria. Marcile⁷ reports a case of anuria of five days' duration. The patient had had renal colic nine years before on right side, and eight days before on left side; uræmic symptoms were pronounced. Nephrotomy was made immediately on the left side; the dressing was

¹ PROGRESSIVE MEDICINE, December, 1900, p. 79.

² Münchener med. Wochenschrift, 1901, No. 2.

³ PROGRESSIVE MEDICINE, December, 1900, p. 79.

⁴ Archiv f. klin. Chirurgie, Band lxiii.

⁵ Annales des Mal. des Org. Gen.-Urin., 1900, p. 1101.

⁶ Ibid., 1900, No. 42.

⁷ Op. cit.

wet with urine the same evening, and the patient recovered. Five months later the patient died of pneumonia. The right kidney (seat of colic nine years earlier) was completely atrophied, a large stone filling the pelvis; the ureteral lumen was obliterated. The left kidney (operated) was hypertrophic and healthy.

Marcile says that this case illustrates the fact that so-called reflex neurotic anuria has been found, in all cases autopsied, to have occurred in patients with only one working kidney; hence it is more reasonable to consider it of mechanical rather than of reflex origin. Uræmic symptoms from anuria occur much earlier when the kidney is healthy; in nephritic cases the organism has become accustomed to the toxic materials.

Klemperer¹ records a case of anuria, which he considers hysterical, in a man, aged sixty-five years. Perusal of the report suggests the possibility that it might have been due, like Marcile's, to mechanical obstruction rather than to hysteria.

Israel² advises nephrotomy for calculous anuria as well as for occlusion of the ureter from other causes, for Götzl has conclusively shown that an increase of urinary pressure in one kidney causes a decrease of secretion by the other. He has performed nephrotomy in five cases of calculous anuria, with three recoveries.

Tilden Brown,³ in discussing a fatal case of post-operative anuria, considers the cause of death to have been delayed surgical shock; and advises that when the heart is weak, nitrous oxide with ether or oxygen should be preferable for anæsthesia to ether or chloroform.

Ureteral Catheterization. The use of the ureteral catheter for both diagnosis and treatment of diseases of the renal pelvis, finds extended approval. Stockmann⁴ has in five cases successfully treated pus infections of the pelvis by instillations through the ureteral catheter. Albarran and Hamonic⁵ report further cases of hydronephrosis cured by drainage by means of the same instrument. Albarran says that in nearly every case of surgical renal disease treated at the Necker Hospital the ureteral catheter is introduced prior to operation. Even tuberculosis of the bladder does not prohibit this procedure.

Catheterization of each ureter acquires added importance in the most recent attempts to estimate the working capacity of a kidney prior to operation on its diseased fellow, an estimation which requires absolute separation of the kidney streams before entrance into the bladder.

Cryoscopy. By this term is designated the effort to determine the functional activity of a kidney through the comparison of the freezing-

¹ Therapie der Gegenwart, 1901, p. 47.

² Op. cit.

³ Annals of Surgery, 1901, p. 225.

⁴ Wiener klin. Rundschau, 1900, Nos. 44 and 45.

⁵ Centralblatt f. Krankh. der Harn. und Sex-Org., 1900, p. 490.

point of its secretion as obtained through the ureteral catheter with : 1, the freezing-point of urine from normal kidneys, and 2, the freezing-point of the blood from the individual under observation. Since the freezing-point of a watery solution is lowered by increasing the solids dissolved in it, it follows that urine containing but little solid matter will freeze at a relatively high temperature, while the blood of the same individual—because retaining solids which should be eliminated by the kidneys—will freeze only at a relatively low point.

The clinical application of these principles to the problem of determining the functional activity of a kidney under suspicion is obviously beset with difficulties and inconveniences ; yet the necessity for some means to this end as a preliminary to surgical operations, especially on the kidneys themselves, is so great that much effort has been given to determining the value of the method under discussion. This measure acquires greater importance from the proven unreliability of renal permeability to methylene blue as a basis for deductions as to the integrity of the kidneys.

The discussion of cryoscopy at the Thirteenth International Medical Congress, by Achard, Bernard, Widal, Albarran, and others, emphasized these propositions : (1) The freezing-point of the blood, notably depressed in cases of renal sclerosis, can be raised in the presence of chronic parenchymatous nephritis ; (2) the freezing-point of the urine, which may be normal or slightly elevated in parenchymatous nephritis, is much higher in cases of renal sclerosis, even approximating that of the blood-serum itself. Hence (3) inferences as to the condition of the kidneys are justified only by a consideration of the freezing-point of both fluids, as well as of the total quantity of urine.

Diminution of renal permeability to methylene blue does not prove a renal lesion ; it is noted with some, especially renal sclerosis, but not in all. Uræmia can coexist with permeable kidneys. Uræmia, renal insufficiency, and renal permeability must be carefully distinguished ; they do not vary in constant ratio, one with another.

Koranyi,¹ to whom cryoscopy owes its inception, summarizes his observations as follows :

Disease of the kidney is accompanied by decrease in the variability of the urine ; insufficiency of the kidney, with decrease in the constancy of blood composition.

Kümmell² presented to the Congress of German Surgeons, in April, 1901, a synopsis of twenty-four operations on the kidney ; in each instance the urine was obtained from the suspected kidney by the ureteral catheter before operation, and the renal disease detected by

¹ *Centralblatt f. Chirurgie*, 1900, p. 505.

² *Ibid.*, 1901, No. 29, Beilage.

cryoscopy and by the elimination of phloridzin. In each case, too, the diagnosis was verified by operation. In seventeen cases the operation was undertaken for hydronephrosis or pyonephritis, in seven for tuberculosis. Recovery occurred in twenty-two of the twenty-four cases, the two deaths not being caused by insufficiency of the renal excretion. In each case the freezing-point of the blood was found after operation to become normal within a few days, though there was usually observed a transient post-operative lowering of the freezing-point of the blood due to the retention of urea. Kümmell does not believe in a "reflex anuria;" he thinks that the decreased excretion that usually follows operation is due to damage to the renal secreting cells by the anæsthetic.

Kümmell's rule in cryoscopy is the following:¹ The freezing-point of normal blood is -0.56° C. or higher; of normal urine -0.9° C. or lower. A freezing-point of the blood of -0.58° C. or lower, or a freezing-point of the urine of -0.8° C., shows a degree of renal impairment which makes operations on the kidney dangerous and unjustifiable. Coincidence of deviation of the freezing-point of the two fluids—that of the blood being lowered and that of the urine elevated—emphasizes the necessity for avoiding operation. It is of course to be remembered that—as Koranyi² asserted in his original article on this subject—abdominal tumors, especially those of the kidney, may be accompanied with a high freezing-point of the urine without actual impairment of the kidney function.

Wiebrecht³ reports a case of tumor in the left renal region; he found the urine normal, its freezing-point 1.35° C., while that of the blood was -0.60° C. The ureteral catheter showed that all the urine came from the right kidney. The tumor was removed and found to be a malignant struma of the left kidney, weighing two pounds. The health improved; the freezing-point of the urine became 1.41° C., of the blood -0.58° C.

Wiebrecht accordingly suggests that the freezing-point of the blood compatible with satisfactory renal function must be lower than has hitherto been asserted.

The proper interpretation of Wiebrecht's observation would seem, however, to be that renal tumors may affect the freezing-point of the blood—as they do of the urine (Koranyi)—without diminishing the aggregate secretory function of the kidney tissue.

Estimation of Renal Function through the Administration of Phloridzin. This method differs radically from that dependent upon the escape of methylene blue through the kidneys, for the latter sub-

¹ Archiv f. klin. Chirurgie, Band lxi., Heft 3.

² PROGRESSIVE MEDICINE, December, 1899.

³ Centralblatt f. Chirurgie, 1900, No. 52.

stance, it has been shown, may appear in the urine without secretory activity of the renal epithelium, while phloridzin, according to present information, is transformed into sugar by the secreting cells of the kidney, probably those of the convoluted tubules. In case of disease of these structures the transformation fails to take place just in proportion to the lesion of the secreting cells; while the prompt appearance in the urine of sugar in amount corresponding to the phloridzin injected shows the integrity of the secreting epithelium (Seelig¹).

The clinical tests of this principle have not as yet been numerous. Casper and Richter² assert that the sugar excretion parallels that of urea and the molecular concentration of the urine; and that it is less in a given time from a diseased kidney—chronic nephritis, pyelonephritis, tumor—than from the opposite healthy organ, the urine being collected by the ureteral catheter. In April, 1901, they presented to the German Congress of Surgeons³ a report of fourteen cases in which this test had been applied; in twelve of these cases the diagnosis of the renal formation was compared with operative or post-mortem findings. Ten of the twelve were operated, and all recovered (though one still has pyelitis on the side not operated); in the remaining two operation was deemed unsafe because the phloridzin test showed serious impairment of the renal function—a conclusion verified in each case by the autopsy.

Casper and Richter emphasize the importance of estimating the three factors—quantity of urea excretion; amount of sugar excretion after injection of phloridzin, and cryoscopy—as a preliminary to operation in cases of suspected renal insufficiency; and they express the utmost confidence in the conclusions based upon these premises. Kümmell supported this position with an experience of twenty-four cases.

Simonelli⁴ asserts that a reliable test of the renal functions is found in a comparison of the time required for the appearance of ingested iodine in the saliva and in the urine; that it appears in both secretions simultaneously when the kidneys are normal; while in cases of renal disease its detection in the urine is delayed remarkably, even five to eight hours in some cases of chronic nephritis. His work does not seem to have been repeated by others as yet.

Suarez⁵ records an observation which has an important bearing on all methods for the estimation of the functional integrity of the separate kidneys. He states that the presence of the cystoscope in a sensitive

¹ Deutsch. med. Wochenschrift, 1900, No. 44.

² Berliner klin. Wochenschrift, 1900, No. 29.

³ Archiv f. klin. Chirurgie, Band lxiv., Heft 2.

⁴ Annales des Mal. des Org. Gen.-Urin., 1900, p. 1194.

⁵ Centralblatt f. Krankh. der Harn. und Sex. Org., 1900, p. 510.

bladder usually inhibits the expulsion of urine from the ureters ; hence, that the proper way to ascertain the functional activity of either kidney is to catheterize the ureter, and then to withdraw the cystoscope, leaving the catheters in position for a prolonged period. He illustrates with a case of pyelonephritis in which the cystoscope failed to reveal any escape of urine from the ureters in five minutes' continuous observation, while the ureteral catheter immediately thereafter showed such escape at regular, short intervals.

While universal experience shows that the presence of the cystoscope in the bladder does not, as a rule, prevent the peristalsis of the ureters, yet there are many clinical observations indicating that the secretory activity of the kidneys is susceptible to variation through influences affecting directly the bladder-neck.

Thus Brown,¹ in discussing post-operative anuria, calls attention to the susceptibility of the kidney to reflex stimulation from the lower urinary tract ; and he mentions as an instance that he has repeatedly observed "a seemingly unnatural retardation of the flow (from the ureteral catheter) so marked in one case as to have aroused the suspicion that the ureter was occluded."

THE BLADDER.

Hernia. Alessandri² presents an elaborate historical, experimental, and clinical essay on hernia of the bladder, which summarizes the present knowledge of this lesion.

Exstrophy. Hartley³ furnishes a complete and critical summary of bladder exstrophy.

Halsted⁴ performed a vesicosigmoid anastomosis in a boy, aged five years, using a bone coupler and the method demonstrated on dogs by Frank.⁵ The patient died of shock sixteen hours later. So far as could be inferred the anastomosis would have directed the urine completely into the rectum.

E. J. Senn⁶ made the first successful vesicosigmoid anastomosis for exstrophy yet recorded. The patient was a young adult ; the anastomosis was made by sutures only, in two stages, and resulted in the diversion of the urine into the rectum. Subsequently the anterior defect of the bladder was closed, there remaining only a pin-hole open-

¹ *Annals of Surgery*, 1901, p. 236.

² *Annales des Mal. des Org. Gen.-Urin.*, 1901, January, February, and March.

³ *Annals of Surgery*, July, 1901.

⁴ Peterson, *Transactions of the American Gynecological Society*, 1900.

⁵ *Journal of the American Medical Association*, 1899, p. 132.

⁶ *Chicago Medical Recorder*, 1901, p. 386.

ing, to obliterate which another operation will be performed (personal communication).

This operation of Senn's seems the most practicable and promising yet offered for the relief of bladder exstrophy.

Peterson,¹ in an elaborate historical and experimental research, presents a résumé of the various attempts to effect successful anastomosis between the ureters and bladder or the rectum, directing especial attention to the effort to prevent infection of the upper urinary tract. Some of his conclusions are: 1. All efforts to prevent ascending renal infection in animals or in man where the ureter has been implanted in the bowel without its vesical orifice have proved futile; the patient may die in a few days of pyæmia, or in a short time of pyelonephritis, or in rare cases may recover from the infection, with resulting contracted kidneys. Hence this operation is not justifiable. 2. The results of the formation of vesicorectal fistulæ have hitherto been unfavorable because of the same resultant ascending infection. 3. The primary mortality of transplantation of the trigonum, including the ureteral orifices, into the bowel has been relatively low (14 per cent.); and the ascending renal infection is either absent or of such a type as to be usually overcome by the tissues. This is, therefore, a justifiable surgical procedure. 4. There is no valve guarding the vesico-ureteral orifice; nor does the circular muscle layer of the ureter, nor the bladder muscles themselves, act as a sphincter.

Rupture. The absence of symptoms indicating peritonitis after intraperitoneal rupture of the bladder is again illustrated in the case reported by Blumer.² On the sixth day after the injury there was found extensive dulness on percussion over the abdomen; a catheter introduced into the bladder gave exit to 196 ounces of bloody urine, whereupon the percussion dulness disappeared. Although there were no signs of peritonitis or other serious lesion, the abdomen was immediately opened; an intraperitoneal rent in the bladder wall sufficiently large to permit the passage of two fingers was found and sutured, with complete restoration of the patient and bladder to the healthy state.

Sieur³ observed a patient who was kicked in the abdomen while his bladder was full. Five hours afterward no urine had been passed, and none escaped through the catheter which was then introduced; there was considerable abdominal tenderness. Although no operation was made the patient recovered completely in six weeks.

Sujetinow⁴ saw a laborer who, after a heavy lift, felt severe pains in

¹ Transactions of the American Gynecological Society, 1900.

² British Medical Society, December 22, 1900.

³ Presse Médicale, 1900, No. 44.

⁴ Centralblatt f. Krankh. der Harn. und Sex. Org., 1900, p. 582.

the loins ; there was no blood in the urine. Eight days later he felt a sharp pain in the lower abdomen ; tympanites, subnormal temperature, and rapid pulse quickly developed. The catheter withdrew a quart of brown urine. At the autopsy, three days later, there was found a tear through the entire subperitoneal curve of the bladder, with purulent peritonitis. The author thinks that the first rupture was incomplete ; and that it became complete eight days later.

Alexander's¹ review of the literature of intraperitoneal rupture of the bladder is exhaustive, critical, and valuable. He tabulates forty-five cases, including one treated personally, in which laparotomy and suture were made ; of these, twenty-three died and twenty-two recovered. Noteworthy are the following conclusions : 1. Drainage of the bladder after operation does not materially affect the result. 2. The injection test is "not only unreliable but positively harmful." 3. With the inflation test Alexander has no experience, but is disinclined to consider it valuable. 4. Absolute differential diagnosis between extra-peritoneal and intraperitoneal rupture is not vital, for each requires immediate operation. The exploratory incision may expose the extra-peritoneal anterior surface first, and be extended upward if the exploration reveals an intraperitoneal laceration.

Alexander's advice to operate in every case in which the symptoms indicate rupture, certainly represents the prevalent surgical sentiment, notwithstanding the undoubted recovery of some such cases without operation ; and experience shows that the chance of recovery increases as the interval between the rupture and operative repair diminishes.

Myoma. Ramsay² records the removal of a myoma from the bladder of a woman, aged thirty-eight years. Less than a dozen instances of vesical myoma are recorded, most of these being post-mortem discoveries.

Leucoplasia. Schmitt described to the Thirteenth International Medical Congress two cases which he calls primitive leucoplasia of the bladder. The patients were aged twenty-one and twenty-two years, respectively ; the most prominent symptom was hemorrhage, profuse and repeated. Papilloma was suspected, but the cystoscope disclosed leucoplasia ; cauterization was followed by healing.

Vesical Incontinence. The Gersuny method of relieving incontinence of urine in women by the deposit of paraffin in the submucous tissue of the orifice was tried by Pfannenstiel ;³ the result was an immediate embolism of the lung—fortunately not fatal—but no decrease

¹ *Annals of Surgery*, August, 1901.

² *Philadelphia Medical Journal*, July 7, 1900.

³ *Centralblatt f. Gynäkologie*, 1901, p. 38.

in the incontinence. On the other hand, Kapsammer¹ reports three cases in which the incontinence was abolished by a single injection of 6 c.cm. in each patient. He says that the melting-point of the paraffin should be higher than the body temperature, and that the liquefied paraffin should be deposited, like the middle lobe of the enlarged prostate, under the mucous membrane at the vesical outlet. (Gersuny advised that the orifice be ringed with a series of paraffin deposits, made at successive sittings.)

Stein² presented the results of a series of experiments on animals, instituted to determine the toxicity and the danger of subcutaneous paraffin injections. He found no evidence of intoxication, and that there is no danger of embolism if care be taken to avoid injecting into a vein by detaching the syringe before injecting, and observing that no blood escapes from the needle. He is convinced that paraffin is gradually absorbed and replaced by connective tissue. He describes a case in Bergmann's clinic, in which a deformity of the nose was entirely corrected by paraffin injections.

At the same meeting Eckstein communicated two cases in which vesical incontinence had been successfully treated by Gersuny's method, though he, like Kapsammer, used only 6 c.cm. for an injection, instead of 50, as advised by Gersuny.

The paraffin used in these injections is a mixture of solid and liquid paraffin, which melts at 102° F., or thereabouts; it is drawn up into the syringe in the liquid state, and allowed to cool until it assumes—when forced out through the needle—the form of a thread rather than of a liquid stream. In this thread form it is deposited in the tissues.

Cystoscopy with Air Distention of the Bladder. The obvious advantages to be derived from a direct view of the vesical lining induced the writer, some years ago, to secure the construction of a cystoscope for use when the bladder was inflated with air. This instrument was exhibited to various medical societies, including the American Association of Genito-Urinary Surgeons, in 1894. It was a hollow, short-beaked sound, the beak carrying a mignon lamp whose rays passed out of a window on the further side were reflected from the bladder wall into the open vesical end of the tube, and traversed this hollow tube and a detachable window at the ocular extremity. When the bladder was distended with air its interior could be directly inspected without the loss of light and distortion of image inseparable from the lens system of the ordinary cystoscope.

The utility of this instrument was, however, limited, indeed, almost vitiated, by one defect—the heat emitted by the lamp when properly

¹ Wiener med. Wochenschrift, 1901, No. 8.

² Berliner med. Verein, July 7, 1901.

illuminated; the lack of water to absorb this heat caused such elevation of temperature of the tube as to render its contact with the prostatic urethra unendurable as well as unsafe after a very brief period.

This difficulty has been overcome by a Rochester company, who manufacture lamps for cystoscopic use that can be brilliantly illuminated without seriously heating the instrument. With such lamps the direct inspection of the bladder inflated with air becomes entirely practicable and eminently satisfactory; it supplements and in some conditions supplants the view through the lens system and water. In cases of hemorrhage from vesical growths or renal disturbance, for example, the rapid diffusion of the blood through the water distending the bladder is apt to limit most seriously the utility of the cystoscope; while with air distention and direct inspection the blood, settling to the lowest point of the bladder, permits a far more satisfactory view.

X The later instruments are made so as to be used with or without the lens system, and therefore with water or with air distention of the bladder; the operator can, therefore, with but little expenditure of time and trouble distend the bladder first with water, then with air, and secure the indirect and the direct view through one and the same tube. X

The cystoscope without the lens system, especially the shorter tubes (16 cm.), gives also an excellent view and control of the deep urethra; in fact, the operator can with this instrument inspect the entire lower urinary tract—bladder and urethra—during a single withdrawal of the tube; and he can at the same time distend the anterior urethra with air, thus giving the aero-urethroscopy first practised by Antal.

The "cold" lamp has certainly enhanced the value and the convenience of both vesical and urethral inspection.

THE URETHRA.

Urethrotomy. The discussion of internal urethrotomy at the Thirteenth International Medical Congress disclosed the practically unanimous opinion that urethrotomy, whether internal or external, is merely a preparation for gradual dilatation with sounds, and that it is practically useless in any other light. The serious objections incidental to it—including some mortality—should virtually banish internal urethrotomy from the list of surgical procedures.

Sterilization of Catheters. The problem of the sterilization of silk and gum catheters without destroying the instruments, a subject which has received so much attention, seems to be solved.

Hermann¹ and Mankiewicz² describe a plan which has been extensively used in various clinics with complete satisfaction, clinical as well as experimental.

Any catheter, whatever its material, is immersed in a saturated watery solution of neutral ammonium sulphate (three parts by weight of the salt to five of distilled water); this solution is then heated to the boiling-point. After two minutes' boiling all bacteria are found to be destroyed, while the catheter remains intact. It is then washed with sterile water and kept in liquid paraffin. If the catheter is required for immediate use, it may be introduced so soon as properly cooled, even without rinsing, as the solution is not irritant to the urethra or bladder.

Mankiewicz states that silk catheters are not injured by five hours' boiling in this solution.

THE PROSTATE.

Hydatid Cyst. Bangs³ incised and drained a cyst containing twenty-five ounces of fluid and hydatids, and occupying a position between the bladder and the rectum. He believes that the cyst originated in the prostate. He notes the rarity of such origin (H. Thompson states it is never observed), and quotes from the literature three cases in which the prostatic origin of a hydatid cyst seems certain.

Relation of the Prostate to Fertilization. To determine whether or not the prostatic secretion is essential to the impregnation of the female, Walker⁴ made partial and complete excision of the prostate in rats; this species was selected because in the male rat this gland can be excised without injury to the remaining portions of the genital apparatus. He found that complete excision of the prostate practically destroyed the animal's ability to fertilize the female, though it did not impair his sexual desire or capacity, the production of spermatozoa, or the structure of the testicle.

Hemorrhage from the Prostate. Heelas⁵ injected daily into the urethra a few drops of a watery solution of suprarenal extract (one to twelve) for the arrest of hemorrhage from the prostate, which ceased in a few days. Habgood⁶ gave 5 grains of the extract internally twice a day for obstinate prostatic hemorrhage, which ceased; the patient had alarming palpitation of the heart, which recurred when the remedy was again given to check renewed bleeding.

¹ *Centralblatt f. Chirurgie*, 1901, p. 63.

² *Berliner klin. Wochenschrift*, February 18, 1901.

³ *Annals of Surgery*, May, 1901.

⁴ *Johns Hopkins Hospital Bulletin*, March, 1901.

⁵ *British Medical Journal*, June 8, 1901.

⁶ *Ibid.*, May, 1901.

Senile Hypertrophy. Etiology. Ciechanowski,¹ in a very clear and exhaustive discussion based on extensive anatomical research, repeats his earlier assertion that the senile hypertrophy of the prostate is in no sense a neoplastic process, nor in any way related to neoplasms. The essential cause in all cases is a chronic inflammation of extremely slow progress; the histological result is an increase in glandular or stroma tissue, or (commonly) in both. This inflammatory process may be incited by gonorrhœa, but occurs independently of this infection. The clinical picture of prostatic hypertrophy often exists without the anatomical changes.

TREATMENT. Urotropin and its American congener, cystogen, maintain their value as successful medicinal agents for the arrest of the secondary bacterial infection—cystitis—which constitutes the most frequent and serious sequel to senile prostatic enlargement. These and the irrigation of the prostatic urethra and bladder with weak solutions of silver nitrate—one grain to a pint, gradually increased in strength—every second or third day, secure years of comfort to many prostatitics who, without these agents, would require immediate drainage of the bladder.

ELECTRICAL TREATMENT. Debédât² furnishes an interesting review of the various methods of using electricity that have been employed for the reduction of the enlarged prostate. He also describes a new instrument by which a continuous current of forty to fifty milliampères is passed from one needle to another, both having been introduced into the substance of the prostate. (Casper, using a similar method some fifteen years ago, achieved sometimes distinct improvement, in other cases serious abscesses, and abandoned the plan as unsatisfactory and dangerous.)

TREATMENT BY OPERATIONS ON THE SEXUAL ORGANS. Wood³ collected 150 cases of castration for prostatic enlargement; in 51.5 per cent. there was a decrease in the size of the prostate, while improvement in the local or general condition was observed in 40 per cent. more. Only 4.6 per cent. were total failures.

Of 193 cases of vasectomy, decrease in the size of the prostate occurred in 9 per cent.; improvement in the evacuation of the bladder in 15 per cent.; the residual urine was decreased in 50 per cent.

TREATMENT BY THE BOTTINI OPERATION. Various attempts have been made to place this blind and blundering operation on a scientific basis by bringing the cautery knife within the range of vision in the bladder, and thus securing ocular guidance of the instrument during the

¹ *Annales des Mal. des Org. Gen.-Urin.*, May, 1901.

² *Revue internationale d'Électro-thérapie*, January, 1901.

³ *Annals of Surgery*, September, 1900.

incision. Freudenberg and Bierhoff¹ describe a "cystoscopic prostatic incisor," which is intended to secure this end, being in reality a cystoscope, which permits the simultaneous introduction and use of a modified Bottini instrument. Wassidlo² presents a similar combination of the two instruments.

Experience must decide whether such attempts shall place the Bottini operation among standard surgical procedures.

Freudenberg³ collects 318 cases of the Bottini operation from the literature, alleging "success" in 77.75 per cent., failure in 13.75 per cent., and mortality 8.50 per cent.

Horwitz⁴ reports upon 161 cases of various operations for the relief of prostatic hypertrophy, including 28 of vasectomy, 31 double castration with 2 deaths, 11 suprapubic prostatectomy with 3 deaths, 7 perineal prostatectomy with 3 deaths, 33 Bottini operations without mortality. He is a warm advocate of the Bottini procedure in mild and selected cases.

TREATMENT BY PROSTATECTOMY. Freyer⁵ reports four cases, each patient over sixty years old, in which he performed enucleation of the "entire" prostate through a suprapubic incision. The enucleated glands (cuts of which in natural size accompany his article) weighed up to four and a half ounces. In each case there was complete restoration of the urinary function, and no residual urine was found, although each of the four patients had been dependent upon the catheter for periods up to six years.

Enucleation of portions of the enlarged prostate has been advised and practised for twelve or more years;⁶ yet Freyer seems to have made a substantial advance in that he has definitely determined the anatomical features involved in the enucleation of the detachable portions of the gland. To one familiar with this work it seems impossible to remove the entire organ by enucleation, and such removal would certainly disorganize the bladder-neck and almost certainly lacerate the prostatic plexus of veins which lie within the prostatic sheath. This criticism was presented by Robson, Atkinson, and others in the numbers of the *British Medical Journal* immediately succeeding that of July 20th.

It would seem, however, that Freyer has carried the enucleation of the enlarged prostate to a point which leaves nothing to be desired, from the clinical stand-point. By making the cystotomy in two stages (the first under cocaine) the operator would reduce to a minimum the

¹ *Centralblatt f. Krankh. der Harn. und Sex. Org.*, 1901, p. 571.

² *Ibid.*, April, 1901.

³ *Ibid.*, 1901, p. 513.

⁴ *Philadelphia Medical Journal*, June 8, 1901.

⁵ *British Medical Journal*, July 20, 1901.

⁶ Author's article, *American Journal of the Medical Sciences*, November, 1900.

dangers inevitably associated with the general frailty and renal impairment so commonly found in these elderly men.

In the discussion of the remote results of operative treatment of the enlarged prostate at the Thirteenth International Medical Congress, Harrison alone advocated any of the so-called "sexual operations," asserting improvement in over one hundred cases in which vasectomy had been practised. The dominant opinion decidedly favored prostatectomy, though Freudenberg and others strenuously supported the claims of the Bottini operation. Frisch, formerly an ardent advocate of the Bottini, still uses it, though admitting that it is a blind operation and by no means free from danger.

THE TESTICLE.

Scudder¹ reviews "all recorded cases," 32 in number, of strangulation of the testicle by torsion of the cord. The normal testicle cannot easily be twisted, but the undescended organs are especially prone to torsion (in 15 of 32 the testicle was retained). Strangulation of the testicle may be with difficulty distinguished from a strangulated hernia, especially because a hernia is often present before strangulation occurs. In 28 of these cases the testicle became gangrenous; in 25 primary orchidectomy was made. In the 7 cases which were not operated, sloughing of the testicle occurred in 3, atrophy in 2, and in 2 (which were untwisted) no subsequent history is given.

Yohimbin. Several articles have appeared in European periodicals lauding the alkaloid yohimbin as an aphrodisiac of the first rank; the restoration of sexual potency completely or entirely lost is asserted to have followed a few weeks' treatment, one-tenth of a grain being administered by the mouth three times daily.

Loewy² asserts as the result of observation on animals, that yohimbin causes dilatation of bloodvessels in the male sexual organs and consequent enlargement, often with erection of the penis in the dog, cat, and rabbit.

Berger³ observed the prompt appearance of erections in six of seven patients treated with yohimbin, five of the six successes being achieved in the subjects of paralytic impotence.

Duhot⁴ reports that in eight of ten cases of more or less complete impotence, erections appeared on the fourth or fifth day, and developed into a satisfactory degree of potency.

¹ *Annals of Surgery*, August, 1901.

² *Berliner klin. Wochenschrift*, 1900, No. 42.

³ *Deutsch. med. Wochenschrift*, 1901, No. 17.

⁴ *Annales de la polyclinique cent. de Bruxelles*, 1901, No. 4.

Krawkoff,¹ as the result of an extensive study of the drug's action, states that it causes first an excitation, then a depression of the central nervous system; this second stage may be accompanied by hallucinations, decrease in blood-pressure and cardiac force, and lowering of the body temperature. There occurs a general hyperæmia of the skin and mucous membranes, as well as of the genitals; in animals erections may occur, though without apparent inclination to approach accessible females. In six men, five of them suffering from impaired sexual power, the drug produced neither erections nor desire, but caused toxic effects as above described.

Loewy² criticises Krawkoff's report, ascribing the toxic effects to unduly large doses of the drug. Loewy further states that yohimbin induces erections in castrated dogs quite as promptly as in the unmutated animals; hence the effect is not due to the effects of the drug upon the testicles. He suggests the possibility that yohimbin may restore sexual capacity to men also who have lost the testicles through disease or operation.

One of my own patients stated that after three doses (one-tenth grain each) there was a notable increase in both erection and desire—evidently the result of suggestion; in three others there was noted no change in the genital function, but some depressing effect on the heart.

It would seem therefore, from present experience, that yohimbin has no constant effect in increasing impaired sexual power, but that it has a distinct toxic influence.

¹ *Klinische-Therap. Wochenschrift*, No. 22, 1901.

² *Therapie der Gegenwart*, July, 1901.

ANÆSTHETICS, FRACTURES, DISLOCATIONS, AMPUTATIONS, SURGERY OF THE EXTREMITIES, AND ORTHOPEDICS.

By JOSEPH C. BLOODGOOD, M.D.

ANÆSTHETICS.

THE reading of the *Jahresbericht über die Fortschritte auf dem Gebiete der Chirurgie* for the years 1898 and 1899, vols. iv. and v., and some of the more recent literature, especially the chapter in Prof. H. C. Wood's most recent text-book, impresses one that we have reached a most important period in our practical knowledge of anæsthesia.

Surgeons—at least those who write—are no longer bigoted in expressing their opinion on which is the best and safest general anæsthetic. Local anæsthesia has been accepted as the safer substitute for general anæsthesia when feasible, and the object now is to improve the technique of each method and to demonstrate clearly its proper field in operative surgery.

Spinal anæsthesia must be considered as yet to be in its experimental stage.

Ether and chloroform remain the drugs of choice in the vast majority of instances in which a general anæsthetic *must* be given. Nevertheless, other general anæsthetics have entered the field in competition with ether and chloroform, and are rapidly finding their proper place, such as nitrous oxide in combination with oxygen, air, ether, or chloroform, ethyl-chloride and ethyl-bromide.

Our present knowledge of practical anæsthesia renders it unjustifiable for any surgeon to use any one anæsthetic exclusively.

The safest anæsthesia seems now to depend upon three factors : (1) The choice of the anæsthetic best adapted for the individual to be operated upon and for the character of the operation to be performed ; (2) the best method and technique for producing anæsthesia with the anæsthetic chosen for the particular individual and operation, and (3) a skilful anæsthetist.

Fortunately in the vast majority of operations all of the recognized methods of general and local anæsthesia are comparatively safe ; but,

nevertheless, in a certain number of operations, and by no means a small number, the life of the patient depends upon the proper choice of the anæsthetic and the technique of its administration.

It is with this second group that surgeons all over the world are chiefly concerned, and this is proved by the vast amount of literature discussing both the practical and experimental side of the question.

The various phases of this question are by no means settled, and it is with these that this review is chiefly concerned.

The Change of Views in Regard to the Selection of a General Anæsthetic. As a student and hospital interne in Philadelphia between the years 1888 and 1892 I never saw chloroform administered, and it was the teaching then that it was almost criminal to give chloroform instead of ether except in obstetrics. This view has changed, although with the majority of surgeons in this city ether is still the anæsthetic of choice. Chloroform is being administered more and more in certain selected cases. Prof. H. C. Wood,¹ in 1900, still advises that in the majority of cases ether is the safer anæsthetic, but believes that chloroform is the better anæsthetic for certain operations and when certain pathological changes are present.

In the Johns Hopkins Hospital Surgical Clinic (of Professor Halsted) ether has been and still is the anæsthetic of choice, but in the last few years we have begun to administer chloroform more and more in certain cases. In the Gynecological Clinic of Professor Kelly in the same hospital, first ether, then chloroform, and now ether have been the anæsthetics of choice; but at present in this clinic chloroform is used, on the whole, more commonly than in the Surgical Clinic. Dr. Kelly, even while in Philadelphia, was rather in favor of chloroform. In 1895 he wrote as follows:² "We give chloroform frequently in the Gynecological Department, and, although in a very dangerous atmosphere, I also gave it in Philadelphia a great many times before coming to Baltimore, but always in dread, because Dr. Wood, of the University of Pennsylvania, had said that any surgeon having a death from chloroform should be indicted for murder. The main reason why Philadelphia surgeons are afraid of chloroform is because they do not know how to give it. In abdominal surgery chloroform is better than ether, as it gives a quiet anæsthesia, rapidly produced, and its after-effects are not so disagreeable. My personal preference, save in cases of grave cardiac complications, as a dilated heart, or where there is failure in compensation, is always for chloroform." Hobart A. Hare,³ also living in the "dangerous atmosphere" of Philadelphia, has fre-

¹ Text-book on Therapeutics, 1900, eleventh edition.

² Johns Hopkins Hospital Bulletin, January, 1895, vol. vi. p. 3.

³ A Text-book of Practical Therapeutics, 8th edition.

quently expressed the opinion that chloroform had a much wider field than that given to it by Philadelphia surgeons, although he still teaches that ether is the anæsthetic of choice in a great majority of cases. Dr. John G. Clark, who was the chief anæsthetist in Dr. Kelly's clinic for over a year, first gave chloroform as a rule, but, on account of very threatening symptoms in a number of cases, changed to ether. In Boston, the stronghold of ether, chloroform is now being used in certain cases. In Germany up till 1892 chloroform was uniformly given the preference to ether. Influenced, as most authorities now write, by the statistics and writings of Gurlt, ether was introduced in many of the German and Austrian clinics. Shortly after the introduction of ether German surgeons became impressed with the dangerous and often fatal post-operative effects of ether, which has influenced them somewhat to return to the use of chloroform; but, on the whole, in Germany this vast experience with both drugs has stimulated them to a more careful study and an attempt to ascertain the special field for each drug.

In this country, in the Eastern States, ether is the anæsthetic of choice, yet in the Southern and Western States chloroform is preferred. On this fact H. C. Wood writes:¹ "The assertion that the inhalation of chloroform is less dangerous in tropical than in temperate climates has been made so frequently and so earnestly by various surgeons practising in hot countries, and is seemingly so sustained by statistics, that it is probably correct. It has received a curious confirmation from a study of reported deaths from chloroform by Thomas R. Evans, which appears to show that most of these deaths have occurred during the cold seasons of the year. It is entirely possible that the increased volatility of chloroform at a high temperature facilitates its elimination from the body, and thereby lessens the dangers of its use." In the last few years in these Southern and Western States ether is being used more and more.

To summarize, we find that in different countries, and different sections of the same country, ether or chloroform (one or the other) has become the anæsthetic of choice, for reasons and conditions difficult to ascertain. In the same section of the country, in the same city, and even in the same large hospitals we find surgeons on one hand expressing a preference for chloroform, and, on the other hand, for ether as the anæsthetic of choice. There is, therefore, a very large apparent difference of individual opinion in regard to chloroform and ether. On the whole, it would appear that those surgeons who have had the greatest experience with ether still prefer it, but use chloroform in certain selected cases, while the contrary is true in regard to those whose experience is greater with chloroform.

¹ Loc. cit., p. 107.

This difference of opinion has had without doubt the best possible effect on our observations and investigations of the use of anæsthetics, for now everyone agrees that chloroform and ether both have their immediate and post-operative mortality, and both may produce serious and often fatal post-operative complications. This difference of opinion has stimulated investigators all over the world to attempt to ascertain which is the safer anæsthetic, first, for the normal individual; second, for the individual suffering from various pathological lesions, especially of the heart and the vessels, the lungs, the kidney, and also in those suffering from grave anæmia, shock, grave infection, and those patients extremely weakened by certain diseases; and, third, for the special operative procedure.

This better and more wide-spread knowledge of the dangers and mortality of general anæsthetics unquestionably has led to the introduction and the widening of the field of local anæsthesia.

These important problems are by no means settled. Nevertheless, in the last few years progress, although slow, has been made.

Discussion on Anæsthesia in the Thirtieth German Surgical Congress in Berlin, May, 1901. Mikulicz¹ sums up the question in the following manner: Since Gurlt's narcosis statistics matters have changed very much, and it is now a question (1) in what cases shall general narcosis be substituted for local anæsthesia; (2) if a general anæsthetic must be given, which is the safer for the individual and operation in question? Mikulicz divides cases for anæsthesia in three groups:

I. *Cases in which the indication for local anæsthesia is absolute.* In this group should be included all those operations which can be properly performed under local anæsthesia, whether the general anæsthetic is contraindicated or not, such as the excision of small tumors, tracheotomy, gastrostomy, and other small operations too numerous to mention. This unquestionably is a very wise statement from a surgeon of eminence.

No one can question the fact that general anæsthetics are frequently given when absolutely unnecessary, for operations which could be just as well performed under local anæsthesia, and many of the deaths and serious post-operative complications have occurred in this group of cases. The dangers of a general anæsthetic, although relatively small, are sufficiently great to make its use unjustifiable in any operation which can be properly done under local anæsthesia. Especially is this the truth in the last few years, during which the technique of local anæsthesia has been improved and its field so much widened.

¹ Centralblatt f. Chirurgie, 1901, Band xxviii. No. 29.

II. *Cases in which the indication for general anæsthesia is absolute.* The majority of operations, of course, fall into this group, such as large operations on the head, major laparotomies, and especially the excision of malignant tumors and their neighboring lymphatic glands—all operations practically impossible to perform properly under local anæsthesia and in which the nature of the disease makes the risk of a general anæsthetic justifiable.

III. *Cases in which we are yet in doubt as to which is the safer method of anæsthesia.* In this group local anæsthesia is possible, but recent observations have demonstrated that the realization of the hope that this method is less dangerous than general anæsthesia has not been fulfilled—that is, the shock from the prolonged operation is as great, or greater, than when performed under a general anæsthetic, and observations have demonstrated that the post-operative complications are apparently as frequent and as fatal. In this group Mikulicz includes major operations on the stomach and intestines, free and strangulated hernia, and goitre.

In view of Kocher's unparalleled experience with the extirpation of goitre under local anæsthesia one must hesitate to agree with Mikulicz here. Experience has demonstrated clearly, and it seems to me almost absolutely, the greater dangers of the general anæsthetic in goitre operations, and for this reason, I think, most surgeons would place the struma operation in Group I.

Without doubt the major operations on the stomach and intestine can be performed better under general anæsthesia, but local anæsthesia was substituted with the hope that the mortality from shock and post-operative complications, especially pneumonia, would be decreased and perhaps eliminated, but Mikulicz's statistics disprove this. The number of cases and the mortality of post-operative pneumonia and other lung complications have been found to be greater after local anæsthesia. This will be more fully discussed later on. These observations, however, are very important. The shock, the fright, and the discomforts of local anæsthesia during these long and tedious major operations on the stomach and intestine have made the operation an ordeal that no surgeon or patient would choose unless it was certainly demonstrable that the local method greatly increased the possibilities of recovery. If Mikulicz's observations are confirmed (there are already some confirmations in the literature) both surgeon and patient will be spared this ordeal.

Operations for reducible hernia unquestionably belong in this group. Although many herniæ may be successfully operated on under local anæsthesia, the number increasing with the skill of the surgeon in this method, nevertheless, in a certain number it is almost impossible to

complete the operation under local anæsthesia. Given a patient whose condition does not contraindicate a general anæsthetic, it is yet a question which method should be followed. At the present writing our experience greatly favors local anæsthesia as being practically without danger, while a general anæsthetic even in these healthy individuals has a certain although a very small element of danger. Given a patient with a reducible hernia, for whom on account of advanced age or certain pathological changes a general anæsthetic is distinctly contraindicated, the operation should either be performed under local anæsthesia or not at all.

Although Mikulicz places strangulated hernia in the doubtful group, my own experience would incline me to place such operations in Group I. So far we have been able, with great success since Cushing's publication,¹ to operate on every strangulated hernia with local anæsthesia, and when these cases—greater in number—are compared with those of former years operated upon under general anæsthesia, there seems no question as to the conclusions.

The grouping by Mikulicz is a very important one, and no doubt will stimulate surgeons in the investigation for the safer method in the doubtful cases.

The Immediate Mortality and the Post-operative Mortality and Complications of General Anæsthesia. In studying this question we must immediately classify our cases in two groups: (1) The healthy individual, and (2) the diseased individual. The latter group must be subdivided according to the organ or the organs the seat of the disease.

In the healthy individual, without doubt, a general anæsthetic is dangerous to life. Statistics go to prove that the danger of death during the administration of the anæsthetic, although small, is greater with chloroform. There are numerous cases on record of death under chloroform from both cardiac and respiratory failure in which the autopsy has revealed no pathological condition to explain the death. Such deaths have been recorded under ether, but are distinctly less numerous. In many of these cases of death both from chloroform and ether the question of faulty technique or a distinct unnecessary overdose of the anæsthetic can be brought forward as the cause. In others the most critical judge would have to admit (from the facts as recorded) that it was the anæsthetic itself which produced death, and no fault can be found with the technique or the anæsthetist. Chloroform in the healthy individual, as proven by animal experiments and autopsies on man, produces fatty degeneration of the heart, liver, and kidneys, and

¹ *Annals of Surgery*, January, 1900, p. 1.

this change is considered to explain some of the cases of late death after chloroform anæsthesia. Ether does not produce these changes except, now and then, to a very slight degree. Were we to judge of the comparative dangers of chloroform and ether from these two facts alone in this group of individuals, ether unquestionably would be the anæsthetic of choice, and it is these facts that have influenced surgeons to select ether as their anæsthetic unless especially contraindicated. On the other hand, the post-operative mortality and complications of ether seem greater than chloroform; for example, lung complications, especially acute œdema and pneumonia, thrombosis with or without embolism of the peripheral veins of the lower extremity. Considering all these factors, authorities differ as to which is the safer anæsthetic in the healthy individual. It is my opinion, which seems to be confirmed by the reading of the literature, that in the ordinary healthy individual in whom there is no special contraindication to a general anæsthetic, ether in the vast majority of cases, irrespective of the age or sex of the patient, is the safer drug. However, in certain individuals and for certain operations chloroform seems the better anæsthetic. Very fat individuals, especially men with short necks, as a rule take the ether badly and increase the danger of post-operative complications. Individuals, especially men, who drink alcohol in any form in excess, take both anæsthetics badly, especially ether; in fact, it is sometimes impossible to narcotize them with the latter. In such individuals most authorities agree that chloroform is the safer and better anæsthetic. In operations of long duration, for example, carcinoma of the breast, ether seems to be the safer anæsthetic. Experience in Prof. Halsted's clinic with some 450 cases has demonstrated this. There have been no deaths on the table, and only two post-operative deaths from pneumonia. In one of these cases the patient had lung metastasis. There were four other cases of pneumonia which recovered. All authorities seem to agree that ether is the safer anæsthetic when given by an inexperienced anæsthetist, and this not infrequently happens in surgery. The dangers of both drugs (especially chloroform) are so greatly increased by faulty administration that I believe it will be safer to allow the anæsthetist to give the drug he has had the greater experience with in cases in which there is no special contraindication for either.

The Immediate Mortality of the General Anæsthetic. In the *Jahresbericht*, 1899, Band v., I find recorded 12 cases of sudden death during chloroform anæsthesia and 2 late deaths, and from other sources I have been able to find 7 cases; in all, 23 chloroform deaths. During the same period and in the same literature I find recorded only 2 sudden deaths under ether anæsthesia—1 under nitrous oxide alone, and

1 under a combination of nitrous oxide, chloroform, and ether. Sippel¹ records a death and discusses the question. His patient was a woman, aged twenty-five years. The heart, lungs, and kidneys were normal. The operation consisted of an exploratory laparotomy and the finding of slight tubercular peritonitis. The anæsthetic—chloroform—was given in a special atomizing apparatus (Keppeler), in which the proportion of chloroform and air is accurately adjusted. The time to produce complete narcosis was longer than usual. At the end of fifteen minutes the patient vomited suddenly, became slightly cyanosed; the chloroform, however, was continued. The pulse suddenly became weaker and ceased; the chloroform was removed; respirations failed. All restorative means, even tracheotomy, were rapidly tried without effect. The autopsy was negative. Sippel considered this death due to heart failure from the effect of chloroform, and he remarks that he introduced this special method of the administration of chloroform because its advocates—Keppeler,² Paul Bert, and others—claimed that this danger of chloroform is very much lessened, almost eliminated, when given by the method of exact dosing. After this death, which occurred in 1893, Sippel returned to the drop method of giving chloroform. He was induced to publish his case in 1899 after reading Geppert's article.³ Geppert claimed that his apparatus was an improvement on that of Paul Bert and Dreser, and this method of regulating exactly the dose of chloroform eliminated most, if not all, its dangers. Sippel published his case to demonstrate that Geppert's and other similar methods did not eliminate the dangers of chloroform.

As far as I can ascertain, most authorities agree with Sippel and teach that the open drop method in giving chloroform is as safe and perhaps safer than the more complicated method with various apparatus, and that there is such an individual difference with regard to the amount of chloroform necessary to narcotize that it is impossible to use any special formula. The patient should have air, and plenty of it. The chloroform should be given by the open method and slowly dropped on the ordinary chloroform mask; the narcosis should be produced slowly, with the least possible amount of chloroform. After the narcosis is complete it should be continued in the same slow, careful drop method. The chloroform should never be pushed, and should be immediately removed during vomiting, the development of cyanosis, or any change in the pulse or respiration. Sippel remarks in his case of death that it was a distinct mistake in technique to continue the chloroform while the patient was vomiting and cyanosis was present.

¹ Deutsch. med. Wochenschrift, 1899, twenty-fifth year, p. 720.

² Journal de Pharm. et Chimie, 1885, fifth series, vol. viii. p. 103.

³ Deutsch. med. Wochenschrift, January 25, 1899, p. 433.

It is unnecessary to report in detail the other cases of death from chloroform. In some, as stated before, faulty technique played a large part in its disastrous result; in others, without much doubt, the chloroform itself seemed to be the cause of death. Studied most carefully, one, however, must be impressed that sudden death from cardiac or respiratory failure during the proper administration of chloroform to a healthy individual is a very rare occurrence. Surgeons who give chloroform should not only properly select their cases, but should see that the drug is administered with the greatest care and vigilance.

Late Deaths from Chloroform. Salén and Wallis¹ report two cases and collect a number of similar cases from the literature. Both their patients were apparently strong, healthy women in whom there were no special contraindications for the anæsthetic. The duration of the anæsthesia was from one to two hours, during which there were no complications. One patient died suddenly on the second day and the other on the third day after the operation. In both the autopsy showed nothing but fatty degeneration of the heart, liver, and kidney. These late deaths after chloroform, fortunately, are rare.

Lengemann,² writing from v. Mikulicz's clinic, considers this question: Do the bad after-effects (fatty degeneration of the organs) of chloroform depend upon the technique of the narcosis? From the literature beginning with 1892, Fränkel³ unquestionably proves that fatty degeneration of the heart muscle, liver, and kidney, both in man and in animals, follows the administration of chloroform as a general narcotic. (See Ungar,⁴ Strassmann,⁵ and Ostertag.⁶)

Lengemann, in his investigation, considering these observations as confirmed, concerns himself chiefly with the question whether the bad after-effects of chloroform can be lessened or eliminated by improvements in the technique of narcosis. He used dogs in his experiments, and administered the chloroform with an apparatus devised by Kionka for animals similar to one devised by Geppert⁷ for man. With this apparatus he was able to regulate and record the exact amount of chloroform administered to the animal during certain periods. It is unnecessary to go into the details of his experiments, but it was clearly demonstrated that there was very little difference in the extent and nature of the fatty degeneration of the different organs in dogs narcotized properly and improperly. It was found even after the most ideal narcosis, and

¹ Hygieia, 1899, Band lxi., Heft 2, p. 158.

² Beiträge zur klin. Chir., 1900, Band xxvii., Heft 3, p. 805.

³ Virchow's Archiv, 1892, Band cxxix.

⁴ Vierteljahrsschrift f. gerichtl. Medicin, 1887.

⁵ Virchow's Archiv, 1889, Band cxv.

⁶ Ibid., 1889, Band cxviii.

⁷ Deutsch. med. Wochenschrift, 1899, Heft 27 and 28.

clearly demonstrated that the bad after-effects of chloroform are not prevented when given after the method of Geppert and others. A certain quantity of chloroform must be in circulation before these degenerations in the organs can be produced, but Lengemann found that this quantity is always present in the blood when sufficient chloroform was given to produce narcosis. Repeated narcoses increased the extent of the degeneration. This investigation, added to that already in the literature, compels us to bear in mind this added danger of chloroform, and when compared with the practically negative findings in similar investigations with ether, should influence us in the choice of ether as an anæsthetic except when it is especially contraindicated. It is interesting to note that Lengemann found a leucocytosis, usually about 40,000, in all of his dogs after chloroform narcosis. Lengemann concludes, agreeing with Sippel¹ and others, that the open drop method of administering chloroform is just as safe as the complicated apparatus of Geppert and others. Leppmann,² in a similar experimental research with ether narcosis, confirms the conclusions of Lengemann and others that ether has no such degenerative action as chloroform.

Post-operative Mortality and Complications of General Anæsthesia. If there were no other dangers in general anæsthesia except sudden death during anæsthesia or later death from fatty degeneration of the organs, ether would be distinctly the anæsthetic of choice; but, unfortunately, this is not true. There are certain post-operative complications, especially of the lungs, which not infrequently are the cause of death. Those who favor chloroform as an anæsthetic are inclined to cast upon ether alone the cause of these lung complications. Recent observations have demonstrated that chloroform shares with ether the odium of these results, although the consensus of opinion puts ether in the first place. They also demonstrate that the general anæsthetic, ether or chloroform, is not always the sole cause of these post-operative lung complications, because they have been observed to take place after local anæsthesia.

M. Gerulanos,³ writing from Helferich's clinic in Kiel, considers the subject in a very exhaustive manner. In the pre-antiseptic days these lung complications were much more prominent than at present, as shown in the statistics of Chevers and Erichsen.⁴ The greater number of post-operative complications during this period was unquestionably due to the local and general infection; but even now, when infection of the

¹ Loc. cit.

² Mittheilungen aus den Grenzgebieten der Med. und Chirurgie, 1899, Band iv., Heft 1.

³ Deutsch. Zeitschrift f. Chirurgie, 1900, Band lvii. p. 361.

⁴ Quoted by Silk, Lancet, March 20, 1897.

operative wound so seldom takes place, lung complications, frequently fatal, are still prominent. Previous to 1892, in Germany, when chloroform was the anæsthetic of choice, there is little in the literature on this subject. Influenced by Gurlt's statistics,¹ ether was more extensively used, and at once its lung complications appear promptly in the literature. Mikulicz,² in an article entitled "Chloroform or Ether?" brought up the subject; also, Popper,³ in 1894, made one of the first publications of death from acute œdema of the lungs following ether narcosis, and many others. These authorities record lung complications after ether anæsthesia. Aufrecht,⁴ in 1897, found that lung complications follow chloroform narcosis, although not quite so commonly as after ether. Gottstein,⁵ in 1898, was one of the first to report lung complications after laparotomy under local anæsthesia. He writes from the Breslau clinic of Mikulicz, and reports 27 cases of lung complication following 114 laparotomies, about 15 per cent.; while in 119 laparotomies in the same clinic under general anæsthesia there were but 7 lung complications, or 6 per cent.; but, as Gottstein says, the majority of the graver cases were performed under local anæsthesia. Mikulicz, in 1901 (before the German Surgical Congress), brings the figures up to date. In 1007 laparotomies and operations for goitre under general anæsthesia there have been 7.5 per cent. of pneumonia, with 3.4 per cent. mortality; while in 273 laparotomies under local anæsthesia there have been 12.8 per cent. of cases of pneumonia, with a mortality of 4.8 per cent.

These cases of lung complications following local anæsthesia demonstrate that the nature and extent of the operation, especially laparotomies, operations on the thoracic cavity, the neck, mouth, and jaw, contribute to the lung complications in addition to the general anæsthetic, and it is this group of cases in which lung complications are so common that we have to decide which is the safer anæsthetic. Mikulicz is inclined to feel that a general anæsthetic is better than the local, and unless specially contraindicated is rather in favor of chloroform. It must, therefore, be remembered, then, that there are many other factors in the cause of lung complications besides the general anæsthetic. Ether, as opposed to chloroform, is distinctly more irritating to the membrane of the respiratory tract, and increases to a greater degree the secretion of mucus. And it is these two factors only that make it more dangerous than chloroform.

¹ Verhandl. d. Deutsch. Ges. f. Chir., 1892.

² Berliner klin. Wochenschrift, 1894, No. 46.

³ Deutsch. med. Wochenschrift, 1894, No. 37.

⁴ Nothnagel, Spec. Pathol. und Therapie, Band xiv., Theil ii., Wien, 1897.

⁵ Archiv f. klin. Chir., Band lvii., Heft 2 and 3.

The Etiology of Lung Complications after Operation. Gerulanos¹ concludes :

1. The direct irritating action of the anæsthetic on the respiratory mucous membrane, with hypersecretion. This is more marked in ether narcosis.

2. The toxic effect of the anæsthetic on the bloodvessels, producing dilatation of the vessels, hyperæmia, and œdema of the lungs, with the usual secondary effect on the heart. This is present in both chloroform and ether, and, authorities seem to think, more marked in the latter. This condition favors hypostatic pneumonia, lowers the resistance of the lung tissue to infection, which may take place (a) by inspiration, (b) by infected emboli, (c) by bacteria in the blood.

3. The inspiration of infected material from the secretions of the mouth and pharynx, or vomitus.

4. Infected or non-infected emboli from thrombosed vessels (usually veins) of the site of or in the neighborhood of the operation.

5. Chilling, fright, and shock from the operation, with or without hemorrhage, all lower the resistance of the patient and act as indirect factors in the production of the pneumonia. (Prolonged general narcosis, long exposure of the chest or peritoneal cavity, reduce the temperature.)

6. A general weakness of the patient lowers the resistance and acts as a very important indirect factor.

7. The restriction of respiration, and especially expectoration, by the pain of the abdominal wound or the tight bandage.

The direct irritating action of the anæsthetic on the mucous membrane of the respiratory tract is considered from experimental investigation not to be a very important factor.

Lindemann² and Hölscher³ say that hypersecretion is a more important factor in that it increases the possibility of inspiration of infected material.

The toxic effect of the anæsthetic on the bloodvessels from the anæsthetic circulating in the blood is a very important factor. Lindemann,⁴ in his experiments on animals with ether narcosis, demonstrated this vessel dilatation with hyperæmia and œdema of the lungs and a secondary effect on the heart. This lung œdema is present during and for a number of hours after the narcosis, and Lindemann concludes that it lowers the resistance and increases the possibility of aspiration pneumonia, and may of itself in certain individuals produce hypostatic pneumonia.

¹ Loc. cit.

² Centralblatt f. Allgm. Pathol., 1898, Nos. 11 and 12.

³ Archiv f. klin. Chir., Band lvii. p. 175.

⁴ Loc. cit.

ACUTE ŒDEMA OF THE LUNGS. Hölscher¹ practically confirms Lindemann's experiments. There is no question about the possibility of inspiration of infected material. Numerous experiments on animals have demonstrated this, and autopsy findings of material in the trachea and bronchi confirm it (Lindemann and Hölscher). The danger is increased when there are suppurative inflammations or wounds of the mouth and pharynx. It has been demonstrated that prolonged and proper disinfection of these cavities decreases the danger somewhat.² Larger particles of infected material, especially of vomitus, in ileus, etc., are more dangerous. It is to be remembered that the inspiration of infected material during vomiting may take place without general narcosis.

EMBOLIC PNEUMONIA is independent of the general narcosis, and is due entirely to the nature of the operation and the disease. This has been carefully studied by Gussenbauer and Lesshaft,³ Klemm and Bayer,⁴ and Fischer and Levy.⁵ In strangulated hernia and other forms of ileus, whether the gut is gangrenous or not, the mesenteric vessels, chiefly the veins, are frequently thrombosed beyond the seat of the constriction, and when the constriction is relieved and the gut reduced emboli may form and reach the lung. The emboli of themselves may be infected, and, if so, produce at once in the lungs an area of pneumonia; or, if not infected, the infarct is an area of lower resistance, and may become secondarily infected from bacteria already in the bronchi, in cases of chronic bronchitis, from infected inspired particles or from the blood. These emboli may take place after any operation in which before or after the operation there is thrombosis of the vessels. It is not an infrequent occurrence in gynecological operations to find various infected and non-infected conditions of the pelvic organs. Embolism has been noted after Alexander's operation and operations for inguinal hernia from thrombosis of the spermatic veins. In operations for various infections of the extremities infected emboli from the seat of the infection may be loosened and reach the lungs. It has been noted in extensive head operations (Kocher and others). On the whole, it is much more common after laparotomies. It is not uncommonly noted secondary to phlebitis of the lower extremity, which condition, we know, is more common after laparotomy. The more one studies the records of post-operative lung complications, the more convinced he becomes that

¹ Archiv f. klin. Chir., Band lvii. p. 175.

² von Calcar. Nederl. Tydschr. voor Geneeskunde, Amsterdam, 1899, No. 6; reviewed in Jahresbericht über die Fortschritte auf dem Gebiete der Chir., for 1899, vol. v.

³ Virchow's Archiv, Band cxxiii. p. 335.

⁴ Centralblatt f. Chir., 1899, p. 217.

⁵ Deutsch. Zeitschrift f. Chir., Band xxxii. p. 252.

embolic pneumonia is the chief cause, and explains many of the cases recorded after local anæsthesia.

Chilling, fright, shock, prolonged narcosis, and exposure of the chest and peritoneal cavity are commented upon by all authorities as indirect causes which should be avoided when possible. It is unnecessary to comment upon the increased danger of lung complications in greatly debilitated patients.

Czerny, quoted by Nauwerk,¹ and others draw attention to the possibility that the pain from the abdominal wound or the restriction of the tight bandage on the abdomen and chest greatly inhibits respiration. They find that these patients will not expectorate, and think these factors increase the dangers of lung complications, especially in debilitated patients and those having chronic bronchitis. The absolutely quiet and prolonged dorsal position of the patient, especially when in a debilitated condition, greatly favors hypostatic congestion and its results.

All these causes acting in various combinations may produce bronchitis, bronchopneumonia, lobar pneumonia, acute œdema of the lungs, hemorrhagic infarcts, gangrene, or abscess. Gangrene and abscess fortunately are most rare, and are due to the inspiration of large infected particles or infected emboli, which depend little, if at all, upon the general narcosis.

The general narcotic acts only as a slight irritant, producing hypersecretion, and on the bloodvessels causing hyperæmia and œdema by lowering the temperature, and by increasing the possibilities of inspiration on account of the muscular relaxation.

Over some of the causes of post-operative lung complication we have some control, on others none.

The Choice of the Anæsthetic to Lessen the Dangers of Post-operative Lung Complications. Schultz,² from a careful study of 460 cases of ether narcoses and 193 chloroform narcoses, all for grave operations, finds that lung complications are less frequent after ether narcosis, and recommends it in these prolonged operations on account of its good effect upon the heart and circulation, the absence of fatty degeneration of the internal organs, and the slight injurious influence on the kidney. This question, however, does not seem to be settled.

Measures to Lessen the Possibilities of Post-operative Lung Complications. If the operation is of short duration and can be done under local anæsthesia this should be attempted, especially if the patient is suffering with some lung lesion or is greatly depressed from some grave infection or disease—*i. e.*, strangulated hernia, typhoid perforation, em-

¹ Deutsch. med. Wochenschrift, 1895, No. 8.

² Dissertation, Halle, 1898, Die Aethernarkose der kgl. Frauenklinik zu Halle; reviewed in Jahresbericht f. Chirurgie, 1898, vol. iv.

pyema, or operations like gastrostomy and colostomy for advanced cases of carcinoma.

When a general anæsthetic is necessary it should be given with the greatest care ; if possible, the narcosis should be an interrupted one, and the least possible amount of anæsthetic should be given. This partial and interrupted narcosis is the most important, and is commented upon by a number of authorities ; with it it is even possible to do extensive abdominal operations, especially if the incision is a large one. Both chloroform and ether can be used in this way. It is sometimes better to begin the narcosis with chloroform, as it is less apt to produce vomiting, and change later to ether, which should be continued if the patient does well under this anæsthetic. When the patient does not do well, but the secretion of mucus, cyanosis, or vomiting occurs, it is, on the whole, better to return to chloroform unless there is a distinct contraindication on account of the condition of the heart or the pulse. If the patient is suffering with chronic bronchitis or any other acute or chronic lesion of the lung, chloroform becomes the anæsthetic of choice. Many of these patients, however, take the ether well, with little or no hypersecretion of mucus. If such is the fortunate result the ether should be continued throughout the operation. Ether when well taken seems to be the anæsthetic of choice in long and grave operative procedures, even laparotomies, in debilitated individuals.

There is little to do to prevent the toxic effect of the anæsthetic on the bloodvessels except to diminish the amount of the anæsthetic and the duration of the narcosis as much as possible. It is in these cases that the skill of the anæsthetist and the rapid operator add so much to the probabilities of a successful result.

Much can be done to prevent the inspiration of infected material from the mouth or stomach. Previous to operation the mouth and pharynx should be carefully disinfected. During the operation no material should be allowed to accumulate in the pharynx. This is best accomplished by the lower position of the head, known for a great number of years by surgeons as Roser's position—a position always employed in Prof. Halsted's clinic.¹ Hobart A. Hare² has demonstrated experimentally the correctness of this position—a detail frequently neglected.

Personally, I am of the opinion that the elevated position of the patient—Trendelenburg's position, and, in addition, when excessive mucus is present or vomiting occurs, to pull the head over the edge of the table, allowing the occiput to drop, and holding the jaws forward—should be a routine procedure in all cases in which, on account of the

¹ Johns Hopkins Hospital Bulletin, 1895, vol. vi. p. 4.

² *Ibid.*, p. 1.

nature of the operation and disease or of the condition of the patient, lung complications are apprehended. I was brought to this conclusion by a comparative study of about 500 cases of inguinal hernia in which the operation was usually done in the horizontal position, with an equal number of operations for hemorrhoids and *fistulae in ano*, in which the operation was performed in the elevated position just described. In the latter, lung complications were practically absent, with no mortality; in the former pneumonia was present in about 2 per cent. of the cases of non-strangulated and 8 per cent. in strangulated hernia. We know very little about the cause of thrombosis and emboli, and as yet we are ignorant as to its prevention.

The chilling of the patient can be prevented, but eternal vigilance on the part of the surgeon and the nurses is necessary. Unfortunately, the proper precautions are frequently neglected. The fright and nervousness of the patient can be greatly lessened by thoughtful and judicious care. Shock from hemorrhage in the majority of instances is under the control of the surgeon. It is safer to operate more slowly, with a minimum loss of blood, than rapidly, with a maximum loss of blood. Prolonged narcosis cannot always be avoided; its dangers can be lessened greatly by the interrupted method. Exposure of the chest and peritoneal cavity can usually be avoided or reduced to the minimum by increasing the temperature of the operating-room and the proper protection of the viscera by warm towels, gauze, or sponges. The preparation of greatly debilitated patients for operation is a serious one. If the operation is an emergency, little can be done except subcutaneous infusion before, during, or after the operation. If it is not an emergency something may be accomplished by very careful diet, and in stomach cases by rectal feeding.

In this group of cases under discussion surgeons recommend that the abdominal and chest bands should be loose; the patient after the operation should be encouraged to inspire deeply and expectorate if possible. In very weak patients it will be necessary for the nurse to aid them to keep the mouth and pharynx clean, especially when they vomit. Minute doses of morphine decrease the pain from the abdominal wound, and, on the whole, make respiration easier. Abdominal distention should be prevented if possible by proper means, as it undoubtedly inhibits deep and proper respiration.

In debilitated patients and those whose circulation is feeble the danger of hypostatic congestion and pneumonia is greatly increased. These patients should have their position in bed frequently changed, first on one side and then on the other, and a partially elevated position of the chest and head. The prolonged flat dorsal position should be avoided.

In a certain group of cases, especially all forms of intestinal obstruc-

tion, and in cases where, on account of the emergency of the operation, it has been impossible to have an empty stomach, the stomach should be carefully washed out previous to operation. This can frequently be done better after the patient is in general narcosis.

For extensive operations on the stomach and intestine in which it is possible to have a number of days for preparation Harvey Cushing's¹ advice should be followed. Cushing recommends the feeding for a number of days with sterilized liquid food and water. His experiments on animals and clinical observations have demonstrated that this method diminished greatly the number and virulence of the bacteria in the intestinal canal, and, therefore, the possibility of infection following operation. It is possible in some instances to accomplish sterility of the stomach and upper part of the small intestine.

The Interrupted Ether Narcosis. Kronacher² discusses it under the title "Die Coupirte Aethernarkose." The method, although not new, has taken such an important place in general narcosis that it deserves special notice. It is a method to be used for long operations on patients whose condition makes us especially apprehensive of the dangers of the narcotic, and in operations impossible to perform under local anæsthesia alone. It is justifiable in all prolonged operations where complete narcosis is not necessary. It is the method we usually employ in the Johns Hopkins Hospital Surgical Clinic in the operation for carcinoma of the breast. It is absolutely essential in all operations on the head, face, mouth, pharynx, and larynx where there is constant danger of blood getting into the respiratory tract. In addition, in these operations, the head is always placed in Roser's position. For "interrupted narcosis" it seems better to give the patient a hypodermic injection of morphine (one-quarter to one-sixth of a grain) one hour previous to the operation. Before proceeding with the operation the patient is almost completely narcotized. During the operation the reflexes should always be present. Unless the narcosis is very slight the patients have absolutely no recollection of the operation, and suffer no pain. Some authorities claim that the shock from the operative procedure is greater in partial than in complete narcosis. The majority, I infer, do not agree with this statement. My own experience is greatly in favor of the partial or interrupted narcosis in the group of cases just described. The wonderful results of obstetrical narcosis, which is really an interrupted chloroform narcosis, is important testimony in its favor.

This interrupted narcosis can be combined with local anæsthesia.

¹ Contributions to the Science of Medicine by the Pupils of William H. Welch, Johns Hopkins Press, Baltimore, 1900, p. 543, and Johns Hopkins Hospital Reports, 1900, vol. ix.

² Centralblatt f. Chir., 1901, Band xxviii. Heft 19, p. 489.

The skin incision is made with infiltration method, and the nerve trunks may be injected when met with during the dissection.

The Use of Atropine and Morphine in Conjunction with the Ether Narcosis. The greatest difference of opinion has been expressed on this point. Wyeth¹ advises it in conjunction with chloroform narcosis to stimulate the heart and to quiet the patient. Blake² uses atropine in ether narcosis to diminish the secretion and to stimulate respiration. Reinhard³ uses both drugs in ether narcosis to inhibit the hypersecretion of mucus, which he considers one of the important factors in the cause of post-operative lung complications. He gives the injection one hour before the operation. Ludwig Braun,⁴ on the other hand, believes that a sufficient dose of atropine to have any effect on the secretion of mucus is only an added danger. On the whole, most authorities are against the use of atropine and morphine as a routine in general narcosis.

Ernest Becker,⁵ in his discussion on ether narcosis, writing from the Hildesheimer clinic, gives his preference to ether narcosis, and states that their experience has taught them that lung complications are as common after chloroform. He also condemns the use of atropine. The chief objection he found to ether was the hypersecretion of mucus, and he has been able to reduce this with success in 500 ether narcoses by adding to the ether just before it is used 20 drops of oleum pini pumilionis (one of the turpentine oils). This not only diminishes the secretion of mucus, but is a slight disinfectant, and as the oil is oxidized, oxygen is added to the ether gas. The method impresses one as worthy of trial. Becker states that he has employed this combination on patients suffering from grave lung diseases.

Anæsthetics in Heart Diseases. This subject was discussed before the College of Physicians in Philadelphia on May 1, 1901. Papers were read by Finney, Stengel, Mayo, and Hare (all published in the *American Journal of the Medical Sciences*, August, 1901, vol. cxxii.). Finney finds the literature on the subject very meagre, and from a study of 142 cases he concludes as follows: "In the myocardial affection only do anæsthetics exert any markedly bad effect. In valvular disease their influences is very slight, but yet appreciable. In functional disturbances they are insignificant." Among the 142 cases there were 8 cases of myocarditis; 7 of these were given ether; 5 took the anæsthetic badly; 3 took it well. In 1 chloroform was first administered, but on account of the bad effects—rapid, irregular, weak pulse and disturbed respiration—ether was substituted. Finney records no death which could be attributed to the action of the anæsthetic on the heart.

¹ PROGRESSIVE MEDICINE, December, 1900, p. 115.

² Ibid., p. 116.

³ Centralblatt f. Chirurgie, 1901, Band xxviii. No. 11, p. 299.

⁴ Ibid., No. 17, p. 441.

⁵ Ibid., No. 22, p. 561.

Stengel also concludes that the anæsthetic is more dangerous in the diseases of the myocardium, although in many instances the anæsthetic ether has been well borne. He has had no experience with chloroform. Stengel, however, brings up a very important point that, although the ether may be well taken, and during the operation there may be no apparent evil effect, yet the action of the anæsthetic on the diseased organ may show itself later, and may be the ultimate cause of death. He records such a case.

Mayo also writes that myocarditis is the condition which the surgeon has reason to fear, and calls attention to the fact that previous to operation there may be no physical signs of the condition until revealed by the autopsy. These patients are more apt to die some days after the operation than during the administration of the anæsthetic.

Hare states : " It is a remarkable fact that very few people, even with grave cardiac and vascular disease, die as a direct effect of the anæsthetic. If statistics were looked into it would be found that very few people die from the effect of the anæsthetic in the presence of cardiac disease. A larger number of people die at stool or on going up stairs when suffering from disease of the heart than from the effects of anæsthesia. It will be found that the anæsthetics when skilfully administered usually exercise what might be called a beneficent rather than an evil influence. I am strongly convinced that in the majority of instances when accidents occur during the administration of an anæsthetic the anæsthetic is not to blame for the fatal result, but rather the shock of the operation." Hare teaches that chloroform is a very dangerous anæsthetic in diseases of the myocardium, and that ether is usually contraindicated in grave vascular diseases, in atheromatous conditions, and in high arterial tension due to vascular changes. With these exceptions Hare considers ether by far the safer anæsthetic.

As mentioned by Stengel, we must remember that the effect of the anæsthetic on the heart may show itself as a post-operative pneumonia or acute œdema.

On the whole, we must conclude from these papers that an anæsthetic, especially ether, is not contraindicated in disease of the heart with good compensation ; but in grave conditions, especially of the myocardium, it may be the cause of sudden death either during the operation or some hours or days later, and, on the whole, ether is the anæsthetic of choice.

The authority of H. C. Wood confirms these conclusions. He writes : " The key to the situation is not the valvular lesion, but condition of the muscle, and ether is the anæsthetic of choice." No condition of the heart is, however, an absolute contraindication to the use of the anæsthetic, and under certain circumstances anæsthesia may be produced when the heart is in advanced fatty degeneration. Wood brings for-

ward a very important point in regard to the relation between local and general anæsthesia and the fatty heart. He believes that the shock and nerve strain which attend a major surgical operation with local anæsthesia are more likely to arrest the fatty heart than the same operation under general narcosis.

In my own experience heart complications following anæsthesia and their mortality have been very much less than lung complications. In 15,000 cases of general narcosis in the surgical clinic of the Johns Hopkins Hospital we have so far never experienced a sudden death on the table which could be attributed to the effect of the anæsthetic on the heart. In a few cases (three, I think) we have had an alarming, sudden, but temporary syncope during ether narcosis. These patients had no valvular lesions. Two cases died suddenly after operation—one, twenty-four hours; one, ten days. In both the myocardium showed extensive changes, and the coronary arteries were very much narrowed by atheromatous patches.

The Effect of the Anæsthetic on the Kidneys. As Wood writes: "Thomas A. Emmet was first to report cases of anuria following ether narcosis in individuals suffering from chronic Bright's disease, but we know that chloroform may have the same effect." Both drugs are contraindicated in an advanced condition of nephritis, but if an anæsthetic must be given Wood favors ether.

Hare¹ teaches that ether is not strongly contraindicated in Bright's disease if properly administered.

Elaborate articles on the effects of ether and chloroform on the kidney, as quoted by Wood, have been written by F. Nachod,² Babacci and Behi,³ and Eisendrath.⁴ These observations demonstrate that albumin and casts are found in the urine in about 25 per cent. of the cases. The percentage is slightly higher after ether, but the changes produced by chloroform are much more profound.

In my own experience, deaths following operations associated with anuria or symptoms of uræmia have taken a much more prominent place than cardiac complications, and are almost equal in certain conditions to lung complications.

General Narcosis with Schleich's Mixtures (Mixed Narcosis). The literature on this subject is so meagre that we can conclude that as yet it is not considered by surgeons of much practical importance in our methods of general narcosis. Honigmann⁵ gives an excellent historical résumé of the various kinds of mixed narcoses up to

¹ Loc. cit.

² Archiv f. klin. Chir., 1890, Band li.

³ Il Policlinico, 1896, N. 3.

⁴ Chicago Medical Report, 1896, p. 10.

⁵ Review, Centralblatt f. Chir., 1899, p. 826.

the publication of Schleich.¹ He is chiefly concerned with experimental investigation to confirm or contradict the conclusions of Schleich. Schleich claimed that by the change in the boiling-point of the mixture of ether and chloroform many of the disadvantages and dangers of general narcosis were lessened. Honigmann could not confirm Schleich's conclusions. Selberg,² from an experimental and clinical study, comes to the same conclusion as Honigmann. Schleich's mixtures are difficult and inconvenient to prepare, and Selberg finds that not infrequently the production of narcosis is more difficult than when ether or chloroform alone is used. He was unable to demonstrate that these mixtures had any special advantage.

Braun,³ before the Thirtieth German Surgical Congress, this year, recommends the administration of ether and chloroform by a method different from that of Schleich. He pictures a special apparatus. Ether and chloroform are in separate flasks, but can be given mixed or alone by the adjustment of stoppers. He advises that the narcosis be introduced with both drugs, later turned to ether; the chloroform can be added for a few minutes when necessary, or in some cases pure chloroform can be given. There was no discussion.

Nitrous Oxide, Alone or in Mixtures. Goldman, of New York, is one of the chief advocates of the use of nitrous oxide, alone or in various mixtures, in general narcosis. Among the new methods of anæsthesia that with nitrous oxide seems to have taken the most prominent position. Goldman,⁴ under the title "An Unprecedented Case of Prolonged Anæsthesia with Nitrous Oxide and Oxygen," reports a very interesting observation. The patient was a woman, aged seventy-six years; general condition fair, perhaps anæmic; the operation consisted of extirpation of both breasts and the contents of the axillæ. The duration of the narcosis was two hours and forty minutes. The anæsthetic throughout was nitrous oxide and oxygen. There was no cyanosis, and convalescence was uninterrupted. Goldman states that it is extremely doubtful whether this patient could have stood either ether or chloroform for this length of time. I think the majority of surgeons will not agree with him. It is not an uncommon occurrence to have patients, especially women over seventy years of age, stand prolonged ether narcosis just as well as the patient of Goldman. Nevertheless, this observation demonstrates that a prolonged narcosis can be maintained with nitrous oxide alone. Later⁵ he reports 100 operations, duration one-

¹ *Schmerzlose Operationen*, 4 Aufl., Berlin, 1899.

² *Archiv f. klin. Chir.*, 1901, Band lxxiii. Heft 2, p. 370.

³ *Centralblatt f. Chir.*, 1901, Band xxviii. No. 29, p. 20.

⁴ *Medical Record*, New York, March 3, 1901.

⁵ *American Journal of the Medical Sciences*, June, 1901, p. 674.

half hour to two hours and forty minutes, in which the narcosis in every case was maintained most satisfactorily with nitrous oxide and oxygen. At the same time he describes and illustrates a new apparatus to be used in this method. He mentions no deaths or complications.

Nogue,¹ Flux,² and Gardner³ advocate the use of nitrous oxide and oxygen. In the discussion of Gardner's paper Noble stated that he had observed grave respiratory symptoms, and Buxton was not favorable to its use. Hewitt⁴ states that nitrous oxide and oxygen is a safer combination than nitrous oxide pure or combined with air. Dent⁵ reports a death under nitrous oxide narcosis, but, as Hewitt⁶ writes in the discussion of this case, the anæsthetic in Dent's case was badly selected. The patient, a boy aged twelve years, was in a very critical condition. There was a large abscess beneath the chin, and it was almost impossible to move the lower jaw. The patient died of asphyxia. Any general anæsthetic would have been dangerous in such a case.

Nitrous Oxide and Ether. Before the New York County Medical Society, Goldman⁷ contributed a second paper on this subject. His experience has demonstrated that preliminary anæsthesia by nitrous oxide before the administration of ether has many advantages. It shortens the period necessary to produce complete narcosis and lessens many of the discomforts. Miller⁸ reports 160 cases in which this method was used with excellent results. Brown and Kelly,⁹ of Baltimore, write: "In our experience the method has seemed to possess so many advantages to the patient, operator, and anæsthetist, and so few disadvantages to any of these, that it has become an indispensable part of our operative technique, and that it has proved satisfactory can be easily judged from the fact that after over 200 anæsthetizations with the method our faith in it, instead of diminishing with experience, has increased a hundredfold." Thomas L. Bennett,¹⁰ anæsthetist at the New York and Roosevelt Hospitals, in advocating the use of nitrous oxide alone or in combination with ether, describes a special apparatus. H. W. Carter,¹¹ of New York, advocates the use of Bennett's apparatus.

Nitrous Oxide—Ether—Chloroform Narcosis. W. Hewitt,¹² anæsthetist to the London Hospital, in a paper on some recent developments in the administration of anæsthetics, considered the method of nitrous

¹ *La France Med.*, 1899, No. 49.

² *Practitioner*, November, 1899, and *Lancet*, February 4, 1899.

³ *Lancet*, April 22, 1899.

⁴ *Ibid.*, February 18, 1899, p. 444.

⁵ *Ibid.*, April 8, 1899, p. 959.

⁶ *Ibid.*, April 15, 1899, p. 1053.

⁷ *Journal of the American Medical Association*, March 24, 1900.

⁸ *Annals of Surgery*, 1899, vol. xxx. p. 709.

⁹ *Philadelphia Medical Journal*, November 3, 1900, p. 869.

¹⁰ *Medical Record*, March 24, 1900, p. 524.

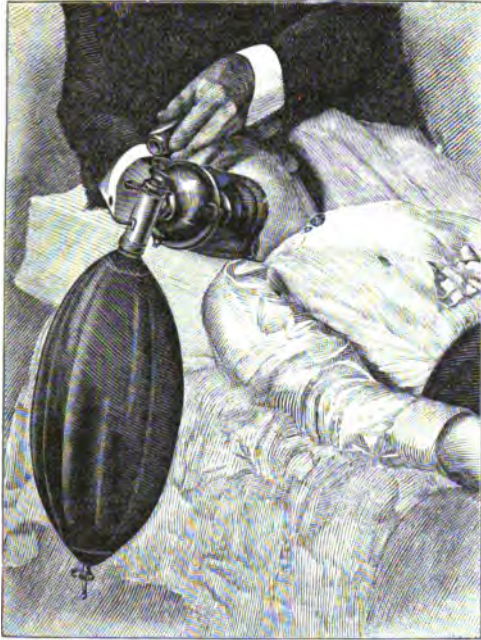
¹¹ *Ibid.*, April 14, 1900, p. 627.

¹² *Lancet*, March 30, 1901, p. 916.

oxide and ether in succession one of the most important. At the same time in certain cases he advocates the substitution of chloroform after full ether narcosis. This method is used chiefly in surgery of the mouth, throat, and nose. Fig. 5 well illustrates the method.

H. C. Wood¹ writes: "Notwithstanding all the evidence which has just been given, there is much reason for believing that nitrous oxide has anæsthetic properties, and that although the unconsciousness which is produced when pure nitrous oxide is inhaled is largely the outcome of the deprivation of oxygen, yet the drug is capable of producing narcosis by its own inherent properties." Of all the anæsthetics, Wood

FIG. 5.



also states that nitrous oxide is the safest. Thus far there have been but four recorded deaths which could with certainty be attributed to the drug. Wood also recommends the combination of nitrous oxide and oxygen.

Ethyl Chloride. Wood and Hare in their text-books on therapeutics do not mention this drug among the anæsthetics. In American literature during the last two years I find but one reference. Martin W. Ware² recommends the following method: The ethyl chloride is sprayed upon a piece of gauze which is situated in a funnel placed on

¹ Text-book on Therapeutics, eleventh edition, 1900, p. 88.

² Medical Record, April 6, 1901.

the patient's face. He recommends it as the best anæsthetic for minor surgery, and claims that the death-rate is 1 in 11,207 cases.¹

In German literature for the last two years I find but four references. Lotheisen² in his first communication discusses 170 ethyl-chloride narcoses; in his second communication³ he reports 850 cases from the Innsbruck Surgical Clinic. There was one death. The patient was an alcoholic, and the autopsy showed extensive disease of the coronary arteries, and Lotheisen believes that the probabilities of a similar result under ether or chloroform narcosis would have been as great. Adding his own cases to those in the literature, this is the first death in 2550 cases. The narcosis is produced by using Breuer's basket—a mask provided with an inspiratory and expiratory valve. Lotheisen emphasizes the importance of such an apparatus. In alcoholic patients, before the narcosis is begun, it is their habit to give a hypodermic injection of heroin muriate. They have used it in the Innsbruck Clinic chiefly in short operations, but it has been found satisfactory even in longer operations. Rohn⁴ reports sixty cases of ethyl-chloride narcosis produced in the dermatological clinic. They were all very favorable. He believes it is valuable for short operations, especially in patients suffering from lung, heart, or kidney affections. Wiesner,⁵ also from the Surgical Clinic in Innsbruck, recommends this narcotic in war surgery. Exactly how many deaths there have been in ethyl-chloride narcoses I am at this writing unable to state; but, as almost every one of these surgeons mentions a death or deaths in the literature, the probabilities are that as yet we have not the correct figures. It is also an expensive form of narcosis except for very short operations.

Ethyl Bromide Narcosis. H. C. Wood⁶ states that Gilles⁷ asserts that in 20,000 successive ethyl-bromide narcoses in Germany there has been no fatal case when a chemically pure bromide has been administered. Nevertheless, Wood states that deaths are recorded by Gleich⁸ and Suarez de Mendoza⁹ when pure bromide of ethyl had been used. Wood expresses the opinion that for short operations ethyl bromide is probably no more dangerous than chloroform; but it must be remembered that an absolutely chemically pure drug should be used, and that this pure drug easily and quickly undergoes chemical changes which

¹ My search in American literature has been by no means exhaustive; I may have overlooked some articles.

² Archiv f. klin. Chir., Band lviii. Heft 4.

³ Münchener med. Wochenschrift, 1900, No. 18.

⁴ Prager klin. Wochenschrift, 1900, No. 21; Review, Centralblatt f. Chir., 1900, p. 975.

⁵ Wiener klin. Wochenschrift, 1899, No. 28.

⁶ Loc. cit.

⁷ Berliner klin. Wochenschrift, 1892, No. 29.

⁸ Wiener klin. Wochenschrift, 1892, No. 5.

⁹ Bull. de l'Académie de Méd. de Paris, 1894.

render it at once dangerous for narcosis. Larisch¹ reports 1263 brom-ethyl narcoses from the surgical clinic in Breslau. There were no deaths and no bad after-effects. He claims that all the deaths reported in the literature were due to the impure drug. He also cautions that it is easily decomposed. Larisch believes that ethyl-bromide is a safer anæsthetic when ether and chloroform are contraindicated. It is especially valuable in short narcoses for the reduction of dislocations and fractures. Garin² reports 1103 cases of ethyl-bromide narcoses for the extraction of teeth. In one case it failed to produce anæsthesia, and chloroform was given. There were no deaths and no bad after-effects.

Paralysis after General Narcosis. It is not infrequent to observe after operation under general narcosis partial or complete paralyzes of one of the extremities. Leszynsky³ believes that in the vast majority—in fact, in almost every case—the paralysis is due to a lesion of the nerve-trunk, and is a peripheral paralysis. He believes that these paralyzes are always preventable and are due to unnecessary pressure, prolonged elevation and extension of the extremity, prolonged and unnecessary position of the patient during the operations, or the use of the clamps or straps retaining the patient in certain positions during the operation. The most important contribution on this subject is a critical and collective review by Flatau.⁴ There are twenty-nine references to the literature. Flatau is of the opinion that the question of etiology is by no means cleared up. There is no reason to believe that the paralysis is ever due to the toxic effect of the drug. That some of the paralyzes may be central cannot be denied, especially in anæmic, arterio-sclerotic individuals. In the majority of instances the paralysis is peripheral, and is due to overextension or prolonged compression of nerve-trunks, the possibility of which is no doubt increased by the muscular relaxation due to the general narcosis.

There is, however, a very practical side to the question. It would appear as if the majority of these cases of paralysis could be avoided by the close attention of the operator and his assistants to the most minute details of the position of the patient and the extremities during the operation. We have observed paralysis of the upper extremities in five instances among about 500 operations, the majority of which were for carcinoma of the breast, the others for removal of glands or tumors in the axilla. In every case in which paralysis followed both the pectoral muscles had been divided. Such a division allows a greater extension of the upper extremity. The dissection along the axillary vessels can be performed to better advantage if the arm is fully ex-

¹ Review, *Jahresberichte f. Chir.* for 1899, Band v. p. 38.

² *Wratch*, 1900, No. 31.

³ *Medical Record*, October 21, 1899, p. 583.

⁴ *Centralblatt f. die Grenzgebiete der Med. und Chir.*, 1901, Band iv. Heft 10, p. 385.

tended. This dissection is usually a long one, and it requires the constant vigilance of the operating surgeon to caution the assistant holding the arm to prevent overextension. I believe that care as to this point will in the future prevent such paralyses. It seems unnecessary to go into the details of how one should prevent unnecessary and prolonged compression and overextension of nerve-trunks during operation. There are sufficient recorded instances of this most annoying complication to compel every surgeon to personally look into the details of its prevention. Fortunately, in our own cases complete recovery has always taken place ; but it is usually a long and tedious convalescence—in one case six months.

Instruction on Anæsthesia as a Compulsory Subject in Medical Curriculum. Coincident to the greater interest taken in the improvement of our methods of anæsthesia in recent years we find a discussion whether anæsthesia is given sufficient attention in the instruction of medical students. Finney¹ concludes his article on "Anæsthetics in Heart Disease" as follows: "In conclusion, I cannot emphasize too strongly my conviction that in every operation the anæsthetist plays almost as important, and in some cases a more important, rôle than the operator ; and one of the reforms most urgently needed in the medical practice of our country to-day is a thoroughly competent corps of anæsthetists in our hospitals, and in our medical schools a thorough and complete course of instruction in the proper methods of administration and use of these agents—so powerful for good when rightly used, so useful in the relief of suffering humanity, and yet capable of producing such disastrous results." Dudley W. Buxton,² anæsthetist in University College Hospital in London, concludes his short article on the same subject with the following remarks: "Practically every medical man in some stage of his career will be compelled to give an anæsthetic, and by far the majority will have to do so very frequently. Admitting this, and admitting the grave danger which attends want of knowledge and lack of experience in giving anæsthetics, it follows that all students should during their training for the profession acquire a competent knowledge of this subject, and should further be compelled to prove their efficiency before being granted a diploma to practice their profession."

Local Anæsthesia. Cocaine is an alkaloid derived from erythroxyton coca, first named by its discoverer, Gardeke, in 1855, *erythroxyline*, but later called cocaine by Albert Niemann,³ who was the first to make a careful study of its physiological action.

¹ Loc. cit.

² British Medical Journal, April 27, 1901, p. 1007.

³ H. C. Wood, Text-book, eleventh edition, 1900.

Solutions of cocaine still remain the most important and the most commonly used to produce local anæsthesia. Other drugs have been introduced as a substitute for cocaine as a local anæsthetic, but thus far they have had a limited field—for example, eucaine A and eucaine B, tropacocaine, holocaine, aneson, nirvanin, orthoform, and ethyl chloride. These will be discussed later.

Rudolph Matas¹ was one of the first to give to American investigators (Halsted, Hall, and Corning) the credit for the subcutaneous method of local anæsthesia with cocaine. In the majority of English and all German literature the credit is given to Oberst and Schleich. H. C. Wood,² in his recent text-book, also gives first credit to the American investigators. To summarize: cocaine was discovered in 1855; its local application as an anæsthetic was introduced by Karl Koller in 1884. Immediately after this Halsted and Hall made numerous experiments with the subcutaneous injection of cocaine solutions, the infiltration of the skin (now usually called Schleich's method), the regional infiltration about the nerve-trunks (now usually called Oberst's method), and the direct injection of nerve-trunks. This work was done in 1884 and 1885. Oberst's and Schleich's first publications were not until 1888 and 1890. The introduction of the elastic bandage as an adjunct to regional anæsthesia was made by Corning in 1885. Schleich's work between 1888 and 1890 seems, however, to have made the most profound impression on the surgical literature of local anæsthesia. It is his development of the local infiltration method and the use of very diluted solutions of cocaine that have widened the field and usefulness of local anæsthesia.

The isolation and direct injection of the nerve-trunk during the operation (the regional intraneural method), although previously performed, was practically introduced by the work of Crile, Matas, and Cushing in 1897.

The Methods of Local Anæsthesia Exclusive of Intraspinal Injections. THE LOCAL APPLICATION OF COCAINE. Almost immediately after its discovery in 1855 cocaine was found to have a distinct anæsthetic action when applied locally to the skin, mucous membrane, or to open wounds and ulcerating surfaces. This was noted in 1862 by Morenoy and Maiz, and in 1880 by von Anrep, and most fully developed in 1884 by Karl Koller.³

At once it began to be used extensively in ophthalmic surgery, surgery of the nasopharynx and larynx, of the urethra and bladder, and in dermatology. Its value when applied in this manner is somewhat

¹ Philadelphia Medical Journal, November 3, 1900, vol. vi., No. 18, p. 820.

² Loc. cit.

³ Wiener med. Wochenschrift, November, 1894.

limited, and as stronger solutions (4 to 6 per cent.) are necessary to produce anæsthesia, the dangers of the toxic effect of the drug are greatly increased. The majority of deaths and threatening symptoms have occurred after the local applications of stronger cocaine solutions to the mucous membrane. With this experience surgeons now use it with the greatest caution, and many have substituted solutions of eucaïne B for cocaine, which seems to have almost an equal anæsthetic effect, but is distinctly less toxic, and it should always, when feasible, be substituted by the infiltration method, with much more diluted solutions. It should also be remembered that when stronger solutions of cocaine are used in this manner it is much safer to have the patient in a reclining position, on account of the danger of sudden syncope due to the action of cocaine on the heart. When eucaïne B is used this position is not necessary.

In many instances the spray of ethyl chloride is as perfect an anæsthetic, and it is practically without danger, and can be used successfully in the majority of minor surgical interventions in the region of the teeth and gums where the local infiltration method is not feasible.

Légrand¹ recommends the combination of a 4 per cent. solution of cocaine added to the ethyl chloride. The mixed solution is sprayed on the skin or mucous membrane, and in five minutes the ethyl chloride has evaporated, leaving the cocaine as a whitish deposit on the surface. This method is most useful when one wishes to apply painful caustics or other applications to ulcerating surfaces and many dermatological lesions; it should be of great value before the application of nitric acid to chancroid ulcers.

LOCAL INFILTRATION METHOD. This was first introduced by Halsted and Hall,² but fully developed by Schleich (*Schmerzlose Operationen*, Berlin, 1894 and 1898: J. Springer). We know, from the work of Liebreich, Halsted, and Schleich, that the production of an artificial œdema of the tissues, especially the papillary layer of the derm, produces a slight anæsthesia, but not analgesia. In 1885 William S. Halsted wrote:³

"1. The skin can be completely anæsthetized to any extent by subcutaneous injections of water.

"2. I have at times, of late, used water instead of cocaine in minor operations requiring skin incision.

"3. The anæsthesia seldom oversteps the boundary of the originally bloodless wheal, but does not always vanish just as soon as hyperæmia supervenes."

¹ Bull. Gén. de Thérap., 1899.

² New York Medical Journal, December, 1884, p. 641; editorial, p. 643, and Halsted's letter, September 12, 1885, p. 294.

³ New York Medical Journal, September 19, 1885, p. 327.

In a personal communication Dr. Halsted informed me that he found normal salt solution less painful than water. I make this quotation in confirmation of Matas' statement¹ that the early American investigators demonstrated the most important points in the local infiltration method. Schleich also demonstrated this property of normal salt solution, but more important were his demonstrations that the most perfect painless anæsthesia could be produced by the proper infiltration of the skin by very weak solutions of cocaine, 0.1 per cent. and less. The key to successful local anæsthesia is the proper infiltration of the skin and other tissues as they are met with in the dissection. The possibility of performing extensive dissections is due to the discovery of the anæsthetic value of the most dilute solutions of cocaine. These solutions can be used almost *ad libitum* with very little if any danger from the toxic effects of the drug. Successful and painless local anæsthesia by this method therefore depends on but two factors: proper infiltration and very dilute solutions of cocaine.

THE TECHNIQUE OF THE LOCAL INFILTRATION METHOD. The success of the anæsthesia depends upon the proper production of a wheal. The fluid should be injected into the skin and not beneath it into the subcutaneous fat. The needle is better introduced in a slight oblique direction; the injected fluid produces an elevation of the epidermis, and the color becomes white (due to anæmia). The first wheal should be a large one. The introduction of the first needle is slightly painful (a very fine one should be employed for the first injections). After this the reintroduction should give no pain. The needle can be thrust along beneath the epidermis, injecting the fluid as it progresses, making a long longitudinal wheal, or it can be reintroduced just within the border of the first wheal, and a successive number of wheals can thus be made throughout the length of the incision. Personally I prefer the latter method, and one should have three or more hypodermic syringes, and with these the successive injections can be made with rapidity. The œdematization of the skin, I believe, can be performed more perfectly, and it is no wider than is necessary for the skin incision, and the anæsthetization of the skin incision is made with the least possible amount of the even very dilute solution, and with this dilute solution it is better to be economical, because in large operations it may be necessary to use very large amounts. When the area of skin incision is infiltrated throughout its length by this method, it is sometimes of advantage to increase the œdematization by injections of sterile salt solution in the same manner. When this is complete the skin incision is always absolutely painless. If the pain of operative pro-

¹ Loc. cit.

cedures were due only to the skin incision every operation could be performed under this method of local infiltration of the skin. Unfortunately this is not true. The deeper tissues are more or less ramified by nerve-trunks and filaments of various sizes, injury or division of which are very painful. The ligation of vessels, especially veins, is painful. To overcome this we œdematize the subcutaneous tissues in the same manner previous to their division. Experience quickly teaches one in what structures this is necessary. Until one has this experience it is always best to infiltrate the tissues before division with the knife. But soon one learns to discriminate. This œdematization is the limit of the infiltration method ; but, as will be discussed later, a dissection of any magnitude cannot be performed painlessly by this method alone ; and that its field is greatly increased by the isolation and direct injection of the nerve-trunks met with during the dissection and these nerve-trunks are not of necessity divided. When the nerve-trunk is too small to be picked out, or is buried in tissue which we do not wish to divide in order to expose the nerve, we anæsthetize the nerve by extensive infiltration about it. So that in the modern operation under local anæsthesia the three methods are combined. It is always a good plan before the clamping and ligation of a vessel, especially a vein, to infiltrate the tissue about it—into the wall of the vessel if possible.

It must be remembered that this infiltration method is tedious ; it must be done with care and gentleness ; during the dissection the tissues must be cut and not torn, and manipulations and tractions must always be limited to the very least amount. Tearing and traction, even when absolutely necessary, constitute the chief pain and discomfort of the local anæsthetic operation.

The fear that local necrosis and reduced resistance of the infiltrated tissues would follow this method, and that infections and suppurations of the wounds would be more common than when the operation is done under general anæsthesia, experience has demonstrated to be without foundation. If the solutions for infiltration are sterile, our own and the experience of others have demonstrated that perfect healing of the wound is just as common. The criticism that the field of dissection is blurred by the œdematous tissue is never made by those who properly follow the method and who have had even a small experience. Proper hæmostasis can be perfectly and painlessly obtained when one follows the precautions to infiltrate about the vessels before they are divided.

The most painful part of the operation is the suturing of the wound. The traction necessary to approximate the buried sutures, especially in laparotomy, is accompanied by some feeling of discomfort, but seldom acute pain. The introduction of the needle into the skin is painful.

This can be almost entirely avoided by re-œdematization from the margin of the skin incision of the area through which the needle is to pass.

REGIONAL PARANEURAL INFILTRATION ANÆSTHESIA. This method consists of the infiltration of the tissues about the peripheral nerves supplying and at a point above the seat of operation. This infiltration produces a perfect anæsthesia of all the structures supplied by the infiltrated nerves. It was first used in operations on the toes and fingers, but of late, through experience and improved technique, it has been extended to the entire extremity, both upper and lower, and for areas on the trunk, head, and neck. It was first practised by Halsted, Hall, and Corning in 1884 and 1885. The method, however, was first extensively used and advocated by Oberst, who published it through his assistant, Pernice, in 1890.¹ According to Braun,² who has used the method extensively, the work of Oberst antedated all others in Germany. Reclus,³ the pioneer worker in local cocaine anæsthesia in France, refers to Krogus⁴ as the originator of this method. At first it was confined entirely to the fingers and toes. Bendt,⁵ Manz,⁶ Hölscher,⁷ and others have used the method for amputations and other operations on both extremities as far as and above the elbow and knee-joints. Thus far a shoulder or a hip-joint amputation had not been attempted by this method.

THE USE OF THE ESMARCH IN REGIONAL PARANEURAL INFILTRATION ANÆSTHESIA. The first object of the elastic constriction was to allow the use of deep injections of solutions of greater strength and of larger amount. The constricting band itself, either due to pressure on the nerves or to the production of anæmia, produces a slight amount of regional anæsthesia. Wohlgemuth⁸ has called attention to the fact that Wolsendorf, in 1676, was able to produce anæsthesia of the limb below a constricting bandage, and under this anæsthesia to perform a painless amputation of the lower third of the thigh. Esmarch⁹ writes that he has performed numerous painless operations on the fingers and toes, producing the anæsthesia by the application of his rubber bandage. According to Matas,¹⁰ Corning¹¹ was first to use the Esmarch bandage in conjunction with this method of local anæsthesia. Oberst seems to

¹ Deutsch. med. Wochenschrift, 1890, No. 14.

² Centralblatt f. Chir., 1897, Band xxiv. No. 17, p. 481.

³ La Cocaine en Chir., Paris, 1895.

⁴ Centralblatt f. Chir., 1894, Band xxi p. 241.

⁵ Münchener med. Wochenschrift, July 4, 1899, vol. xlvi. p. 384.

⁶ Centralblatt f. Chir., 1898, No. 8.

⁷ Ibid., 1899, vol. xxvi. p. 670.

⁸ Deutsch. med. Wochenschrift, 1898, No. 11.

⁹ Archiv f. klin. Chirurgie, vol. xvii. p. 294.

¹⁰ Loc. cit.

¹¹ New York Medical Journal, September, 1885, vol. xlii. p. 317.

have come to the same conclusion independently. There is a good deal of difference of opinion with regard to the value of the elastic constriction. Hölscher¹ does not think it absolutely necessary. On the whole, the majority of authorities agree to its added effect. It unquestionably allows the injection of stronger solutions and of a greater amount of the solution, with less danger of toxic effects, and frequently in this method it is necessary to use larger amounts of stronger solutions. When this is done the Esmarch bandage should be allowed to remain on the limb for at least one-half to one hour. Clinical observations and animal experiments have clearly demonstrated that when this is done the injected cocaine solution loses its toxic effect. Why, we do not know.

Kohlhardt, of Halle,² in his paper before the German Surgical Congress, reported the following interesting animal experiments: When he injected a toxic dose of cocaine in an extremity and removed the Esmarch, in fifteen minutes or less all the animals died; if the Esmarch was removed between one-half and one hour, the animals exhibited toxic symptoms of decreasing severity, but none died. If the Esmarch was left on an hour or more there were no toxic symptoms.

THE TECHNIQUE OF THE REGIONAL PARANEURAL INFILTRATION ANÆSTHESIA. The constricting bandage is placed about the extremity at a short distance above the seat of operation, the base of the toe or the finger, the hand, the foot, the wrist or the ankle, the leg or the forearm, the thigh or the arm. The needle is introduced just below the constricting bandage, and tissues about the nerve are infiltrated; the number of such deep injections depends upon the number of nerves. If properly performed, in five or ten minutes the region supplied by these nerves becomes anæsthetic and allows almost any operative procedure to be done painlessly. The anæsthesia lasts for some time. The Esmarch should be left on for a period, the duration of which should correspond with the amount and the strength of the solution used. If weak it can be removed at once. As will be discussed later, this method is better combined with the local infiltration of the skin and the direct injection of the nerve. When so combined the weaker solutions of cocaine can be used. The Esmarch may be discarded entirely, or if applied can be removed as soon as the operation is over.

The application of the Esmarch is somewhat painful. This is lessened by using a broad rubber bandage and constricting just enough to occlude the vessels. As a rule, the pain increases with the duration that this constricting band is left in place.

¹ Loc. cit.

² Centralblatt f. Chirurgie, 1901, Band xxviii. No. 29, p. 23.

THE REGIONAL INTRANEURAL METHOD. This may be done as Crile and Matas¹ suggest for operations on the extremities, especially for amputation. The nerve-trunk is exposed under the infiltration method and then injected with a 1 per cent. solution of cocaine. Properly performed, this blocks all afferent impulses (see *PROGRESSIVE MEDICINE*, December 1899 and 1900). In a few minutes there is regional anæsthesia in the areas supplied by the blocked nerves. In Cushing's² method the nerve-trunk is injected as it is exposed during the dissection. Cushing elaborated the technique especially for hernia operations, but it is equally well adapted for many others. Matas³ calls attention to the fact that the paralyzing effect of cocaine upon the nerve has previously been extensively studied by U. Mosso,⁴ and later by C. A. François Franck.⁵

In making the intraneural injection experience has demonstrated that 0.5 to 1 per cent. solutions are required. Bieberfeld⁶ has demonstrated this by means of experiments on animals, using distilled water, salt solution, and various cocaine solutions. He concludes that cocaine is indispensable in the production of anæsthesia by intraneural injection, and advises that a physiological salt solution with 0.25 to 0.5 per cent. solutions of cocaine be used.

THE MIXED METHODS OF LOCAL ANÆSTHESIA. As a matter of fact, in almost every operation perfect local anæsthesia is better accomplished by the combination of the three methods just described—infiltration, paraneural and intraneural injections.

As a preliminary step to every operation under local anæsthesia all authorities agree that it adds to the success of the method to give morphine hypodermically. Doses varying from $\frac{1}{8}$ to $\frac{1}{4}$ of a grain should be given from one-half to one hour previous to the time of the operation. This can be repeated just before and during the operation in patients who are unusually hypersensitive. One, however, should avoid an overdose of this drug.

Two or more local anæsthetics may be used during the same operation, as cocaine with eucaine B, ethyl chloride, nirvanin, etc. This combination is chiefly employed in operations of long duration, with the hope of lessening the danger of the toxic effects of cocaine. As a rule, this is hardly necessary when very dilute solutions of cocaine are used. It is sometimes necessary to give during the local anæsthetic operation interrupted general narcosis; chloroform is usually preferred.

¹ Loc. cit.

² *Annals of Surgery*, January, 1901, p. 1.

³ Loc. cit.

⁴ *Gior. della R. acad. di Med. di Torino*, ser. iii., xxxviii.

⁵ *Archiv de Physiologie normale et physiologique*, 1892, vol. iv. 5-me serie.

⁶ *Archiv Internat. de Pharm. et de Ther.*, vol. vi. fasc. 5 and 6; *Centralblatt f. Chir.*, 1900, Band xxvii. No. 15, p. 411.

This has been called by Schleich and Cushing "the morphine-cocaine-chloroform anæsthesia."

During the entire operation an assistant should stand by the head of the patient, not only to watch and record the pulse and respiration, but to carry on, if possible, a conversation, with the hope of distracting the patient's attention from the discomforts and details of the operative procedure. This has been well named by Lilienthal¹ "moral anæsthesia." Properly performed we have found it a distinct aid. I have found the use of aromatic spirits of ammonia as a "smelling salts" very gratifying to the patient during the painful periods of the operation.

The proper combination of the various methods of local anæsthesia, with and without the interrupted ether or chloroform narcosis, has most successfully extended the field of the local anæsthetic operative procedures and lessened the danger of general narcosis.

Bloch² is one of the chief advocates of the mixed method in local anæsthesia plus interrupted chloroform narcosis. He advocates it especially for major and long operations in which experience has taught the danger of complete general narcosis. He employs ethyl chloride as a local anæsthetic, and states that he has reduced the amount of chloroform on an average of from 6 to 1 grain (total amount used). In some cases the general narcosis is first given, in others the local. He reports some 393 operations by this combined method.

Hölscher³ advocates the use of the ethyl chloride spray previous to the local infiltration and regional paraneural injection in operations after Oberst's method, and he frequently combines cocaine and eucaine, each in solution of 0.2 per cent. With this combination he has been able to do much higher amputations of the extremities.

Gonka⁴ advocates the combination of the electric current with the cocaine solution. This solution (4 per cent.) is applied to the skin surface by saturating a piece of gauze, and then the current—about 10 milliamperes—passed through the part for ten minutes. The anæsthesia is perfect. I mention this method, as further experience may demonstrate that it will allow us to take large skin-grafts from the thigh without the aid of general anæsthesia—an operative procedure so far not satisfactory under the other methods. The duration of the anæsthesia, according to Gonka, is practically only about five minutes—sufficiently long, however, to cut a large graft.

¹ *Annals of Surgery*, 1898, p. 58.

² *Nordeiht medicinsht Arkiv*, 1899, Band x. No. 33, and *Revue de Chir.*, 1900, No. 1; *Centralblatt f. Chir.*, 1900, Band xxvii. No. 14, p. 384.

³ *Münchener med. Wochenschrift*, 1899, No. 8.

⁴ *Centralblatt f. Chir.*, 1900, vol. xxvii. No. 4, p. 94; and *Przeglad lekarski*, 1899, Nos. 40-42.

OTHER LOCAL ANÆSTHETIC DRUGS. These have recently been fully discussed in an elaborate article by Pouchet.¹

Eucaïne A should be mentioned only to be condemned, on account of its toxic properties, which are very much like strychnine poisoning.

Eucaïne B, introduced by Silex in 1897, is unquestionably the most important substitute for cocaine. It is not quite equal to cocaine in its anæsthetic action, but is distinctly less toxic. Most authorities advise that when stronger solutions are necessary, or when large amounts of less strong solutions are required, eucaïne B is, on the whole, the safer substitute for cocaine. It has almost replaced cocaine as a local application to the mucous membrane in operations on the urethra and bladder. It can be used here in large amounts in a 4 per cent. solution. I believe that it would be a safer substitute for cocaine as a local application to the mucous membrane of the nasopharynx and larynx. It is a good substitute for cocaine in Oberst's paraneural infiltration, especially in the more extensive operations higher up on the extremities, in which the weaker solutions of cocaine are less reliable. We may find that it is equally efficacious for intraneural injections where 1 per cent. of cocaine is usually employed—a solution of cocaine too strong to use extensively without danger of toxic symptoms.

Heinz,² Braun,³ Hölscher,⁴ and Barker⁵ advocate the substitution of eucaïne B for cocaine in all operations.

The consensus of opinion, however, seems to agree with Schleich—that if it is possible to perform the operation with 0.1 per cent. or less solutions of cocaine, that this drug produces the better anæsthesia. However, should toxic symptoms appear before the completion of the operation it will be safer, if any more anæsthetic is required, to use eucaïne B. According to many authorities, the sterilization of eucaïne B by boiling does not injure its anæsthetic properties, while the contrary is true of cocaine solutions. Our own experience with the sterilization of cocaine solutions by the fractional method (steam sterilizer) has had no appreciable effect upon its anæsthetic properties. Further investigation is needed on this point.

Bier,⁶ in his recent second communication on spinal anæsthesia, also advises the substitution of eucaïne B for cocaine for spinal anæsthesia, on account of its less toxic properties.

Tropacocaine is advocated by Custer⁷ in a most elaborate publication.

¹ Le Progrès Medical, 1899, Nos. 16 and 17.

² Virchow's Archiv, 1898, Band cliii. Heft 3.

³ Archiv f. klin. Chir., 1898, Band lvii. Heft 2.

⁴ Loc. cit.

⁵ Lancet, January 20, 1900, p. 156.

⁶ Archiv f. klin. Chir., 1901, Band lxiv. Heft 1, p. 236.

⁷ Basle, B. Schwabe, 1898, and Münchener med. Wochenschrift, 1898, No. 32.

He claims that this drug has similar advantages over cocaine as eucaïne B. Pouchet and other authorities do not mention it.

Aneson is recommended by Mosbacher¹ as a substitute for cocaine because it is always sterile, is less toxic, and there are no after-pains.

Nirvanin is recommended by Luxenburger.² *Holocaine* and *orthoform* are both rejected by Pouchet because their action is not uniform.

Our best American authority, Matas,³ writes that eucaïne B and nirvanin alone among these many drugs "deserve to be classed as 'succedanea' of cocaine. Because of lesser toxicity and their capacity to stand boiling without decomposition, and for other reasons, they may be utilized with advantage alone or in conjunction with cocaine; in this way, while not superseding cocaine, they have undoubtedly contributed to widen and diffuse the practice of local anæsthesia."

THE DOSE AND PREPARATION OF THE COCAINE SOLUTION. The majority of authorities advocate the employment of 0.1 per cent. or less solution of cocaine for infiltration, and 0.5 to 1 per cent. solution for intraneural injections. These solutions should always be made up with 0.2 per cent. of sodium chloride. The solution in most common use is Schleich's No. 2:

Cocainæ muriat.	0.1
Morphinæ muriat.	0.02
Sodii chlor.	0.2
Aqua destillata	ad 100.00

It is a question whether the morphine is absolutely necessary. Custer⁴ claims that it is not. It is my rule, when very large amounts of the solution are necessary in the infiltration of the deeper tissues, to use a similar solution prepared without morphine, and diluting this solution, as the operation grows more extensive, with sterile salt solution. Our solutions are sterilized by steam. Matas drops the tablet prepared by several manufacturers in boiled water, and then heats the solution nearly to the boiling-point, repeating this procedure two or three times. This seems to be the most practical and simplest method. For every operation under local anæsthesia one should have at least three sterile solutions, Schleich's No. 2, 1 per cent. solution without morphine, but in salt solution. These can be poured from their sterile flasks into medicine glasses previously boiled.

Spinal Anæsthesia. REGIONAL ANÆSTHESIA BY SUBARACHNOID COCAINE INJECTION—LUMBAR PUNCTURE. In PROGRESSIVE MEDICINE for December, 1900, Quincke's method of lumbar puncture was described, quoting from his original article. This operative procedure,

¹ Münchener med. Wochenschrift, 1899, No. 3.

² Ibid., Nos. 1 and 2.

⁴ Loc. cit.

³ Loc. cit.

which has become such an important one both for diagnostic and therapeutic purposes, was discussed. Its most important application—the production of regional anæsthesia by injection of cocaine in the sub-arachnoid space, reintroduced in 1899 by Bier—was only mentioned. The further discussion was postponed until this year, on account of space.

The literature of lumbar puncture should date from the work of Corning, of New York, on account of his first publication, in 1885 (“Spinal Anæsthesia and Local Medication of the Cord,” *New York Medical Journal*, October 31, 1885). Although Corning made additional publications in 1886 (*Pain*, New York, 1886, and *Local Anæsthesia*, Appleton, 1886) and in 1888 (*Medical Record*, p. 291), his work does not seem to have made the impression it should upon the profession either in this country or in Europe. The importance of lumbar puncture as a diagnostic and therapeutic procedure, according to all authorities, dates from Quincke’s “epoch-making contribution”¹ in 1891 and second publications in 1891 and 1895.²

In 1898 there was an exhaustive review of the literature of lumbar puncture by Neurath,³ and, recently, in October, 1900, a critical summary by Alfred Hand.⁴

THE LITERATURE OF SPINAL ANÆSTHESIA. Although Corning,⁵ in 1885, was the first to use spinal injections of cocaine to produce anæsthesia, the profession did not seem to recognize its surgical application and importance, and for this reason the credit for the “epoch-making contribution” has been given to Bier, whose paper, in 1899, entitled “Experiments with Cocainization of the Spinal Cord,”⁶ was at once recognized by the entire surgical world. Bier in this article referred to Quincke’s method of lumbar puncture, and writes that he used it in introducing the cocaine. Neither Quincke nor Bier seems to have had any knowledge of Corning’s original publication.

In May, 1900, there is a collective review by Hahn,⁷ of Vienna. In this first year following Bier’s publication Hahn was able to collect 18 references of nine authors (Corning not included). Tuffier, of Paris, was the most enthusiastic follower. In April, 1901, there is a second collective review (Corning included) by Hahn,⁸ in which, although but two years have elapsed since Bier’s publication, Hahn was able to

¹ Verhandlungen des Congresses für innere Medicin, 1891, vol. x.

² Berliner klin. Wochenschrift, 1891, No. 38, and 1895, vol. xxxii.

³ Centralblatt f. d. Grenzgeb. d. Med. und Chir., 1897, 1898, vol. i.

⁴ American Journal of the Medical Sciences, October, 1900, vol. cxx. p. 463.

⁵ Loc. cit.

⁶ Deutsch. Zeitschrift f. Chir., 1899, Band li. p. 361.

⁷ Centralblatt f. d. Grenzgeb. d. Med. und Chir., 1900, vol. iii. p. 337.

⁸ Ibid., 1901, vol. iv. Nos. 8, and 9.

collect 128 references, in which there are reports of 1708 cases of spinal anæsthesia, with 8 deaths.

It is interesting to note in Hahn's review that almost one-third of the cases are reported from this country—586 cases, 41 authors; France, 406 cases, 10 authors; Roumania, 227 cases, 7 authors (of these Racoviceanu reports 125); Austro-Hungary, 127 cases; Belgium, 42; Switzerland, 34; Spain, 22; Argentine, 21; and, remarkable to note, Germany reports only 10 cases;¹ Russia, 4; and England only 1. "This one English case," Hahn writes, "strange to say, is the only operation performed above the thorax and for removal of the thyroid gland."²

In American literature the most complete articles are by Matas, Fowler, Goldman, Hopkins, Lee, Rodman, Laplace, Phelps (all in the *Philadelphia Medical Journal*, November 3, 1901, vol. vi.), Murphy,⁴ and a collective review by Patterson.⁵

CORNING'S POSITION IN REGARD TO LUMBAR PUNCTURE FOR THERAPEUTIC PURPOSES AND SPINAL ANÆSTHESIA. When one reads Corning's original publication,⁶ and two recent ones,⁷ he cannot but be impressed that Corning's experimental and clinical work established the possibility of lumbar puncture for therapeutic purposes (he does not discuss its diagnostic value), and the possibility of producing regional anæsthesia, and it would seem to be the fault of the time rather than the work itself that so little or no permanent impression was made upon current literature. The credit for its re-introduction belongs to Quincke and Bier, but these three names should always be associated as the originators in this field.

LUMBAR PUNCTURE FOR DIAGNOSTIC PURPOSES. In *PROGRESSIVE MEDICINE* for December, 1900, the work of Councilman, Mallory and Wright, of Boston, and that of Osler and Fletcher, in Baltimore, was referred to. The former authorities, with a very large experience, state that they have never observed any ill effects to follow lumbar puncture for diagnostic purposes in cerebro-spinal meningitis. The latter record

¹ In Tinker's report of the Thirtieth Congress of the German Surgical Association (*American Medicine*, May 4, 1901, vol. i. p. 197) he writes that Mikulicz has used spinal anæsthesia in forty cases with no deaths, but some disagreeable after-effects. Mikulicz predicts that spinal anæsthesia will be one of the most important methods in the future.

² Barling, *British Medical Journal*, January 5, 1901.

³ Hahn has made a mistake in regard to Barling's case. The reading of the original (*loc. cit.*, p. 18) brings out the fact that the thyroid gland was removed under the local infiltration method, and not by spinal anæsthesia. I am unable to find any reference in the literature to any cases of spinal anæsthesia performed in England.

⁴ *Journal of the American Medical Association*, February 9, 1901, vol. xxxvi.

⁵ *American Journal of the Medical Sciences*, February, 1901, vol. cxxi. p. 227.

⁶ *Loc. cit.*

⁷ *Medical Record*, October 20 and November 17, 1900.

the same experience after seventy-five punctures. Hand,¹ in his critical summary, does not mention any bad effects following the operation. Gumbrecht² (not mentioned by Hand) reports seventeen cases (collected from literature) of sudden death following simple lumbar puncture for diagnostic purposes. In view of the large experience of many other authorities who report very few, in the majority no serious consequences following simple lumbar punctures for diagnostic purposes, these seventeen cases of Gumbrecht are hard to explain. They are sufficient, however, to make both the physician and surgeon cautious in their selection of cases for this operation. Lumbar puncture should not be performed for diagnostic purposes unless it is clearly indicated.

THE DIAGNOSTIC VALUE OF LUMBAR PUNCTURE. By the introduction of a hollow needle into the subarachnoid space and the withdrawal of the spinal fluid we are aided in our diagnosis of the disease (1) by the estimation of the pressure of the fluid in the canal, and (2) by the chemical and bacteriological examination of the fluid itself. As Hand³ writes, there have been many conflicting reports in regard to the pressure in different diseased conditions, due, without doubt, to faulty methods and interpretation. This has been very largely rectified by the work of M. Pfaundler,⁴ which could not be properly discussed here without taking too much space. The chemical and bacteriological examination of the fluid is more important, the bacteriological findings perhaps the most. The demonstration of the specific micrococcus of cerebro-spinal meningitis clinches the diagnosis of the disease. The presence of any pyogenic bacteria in the spinal fluid is a most important factor in diagnosis. Typhoid bacilli have been found in two instances by Lenhartz⁵ and Wentworth.⁶ In regard to the presence of the tubercle bacilli, Monti,⁷ from an experience of fifteen cases, states that lumbar puncture furnishes no help in the diagnosis of tubercular meningitis. He was unable to find the tubercle bacilli in the fluid. Wentworth (from Hand's review) concludes from a general review of the literature that the fault is not the absence of the tubercle bacilli in the fluid, but the technique of the examination. A proper and careful examination should demonstrate the tubercle bacilli in the fluid withdrawn in the majority of cases of tubercular meningitis.

In regard to the presence or absence of sugar, Comba⁸ has found that in normal cerebro-spinal fluid in children there always exists a glucose-like producing substance. In tubercular meningitis the amount of glucose is much less, and soon disappears. In meningitis due to the

¹ Loc. cit.

² Deutsch. med. Wochenschrift, 1900, vol. xxvi. p. 386.

³ Loc. cit.

⁴ Jahrbuch. f. Kinderheilkunde, 1889, Band xlix.

⁵ Congress f. innere Medicin, 1897, p. 15.

⁶ Archives of Pediatr., Nov., 1899.

⁷ Archiv f. Kinderheilkunde, Band xxiv.

⁸ Clinica. Med., 1899.

micrococcus of Weichselbaum, of the diplococcus of Fränkel, glucose is absent in the exudate. An increase in the albumin in the fluid is an indication of inflammation. An amount of albumin above 0.25 per 1000 should be considered an excess. Although in the majority of cases of meningitis, whether tubercular or pyogenic, the fluid is cloudy, now and then in tubercular meningitis the fluid may be clear. A cloudy fluid is at least an indication of inflammation. In cases of contusion of the spine with cord symptoms lumbar puncture may prove to be a very valuable diagnostic and perhaps therapeutic procedure. Jacobi,¹ referred to by Hahn, reports two cases of contusion of the spine followed by paraplegia. "Lumbar puncture removed bloody fluid, and rapid improvement followed."

LUMBAR PUNCTURE FOR THERAPEUTIC PURPOSES. The indications are: (a) To relieve the pressure by removal of the fluid; (b) the removal of the fluid if it contains pyogenic bacteria, not only relieves the pressure, but seems in many cases to be of great value, acting in the same manner as in the drainage of any purulent cavity; repeated lumbar puncture in cerebro-spinal meningitis is considered by many authorities a most important therapeutic agent. It has recently been advocated in tubercular meningitis to irrigate the entire cerebro-spinal subarachnoid space by trephining the skull and the introduction of a trocar through the dura, the second trocar between the lumbar vertebrae. Experimentally this irrigation is possible in animals. The only case in which I have seen it attempted in man failed. Many drugs have of recent years been introduced by the method of lumbar puncture. Corning unquestionably was the first, followed by Siccard, Jaboulay and Jacob (discussed in *PROGRESSIVE MEDICINE* for December, 1900). Hand² mentions others.

LUMBAR PUNCTURE FOR SPINAL ANÆSTHESIA: INDICATIONS, CONTRAINDICATIONS, AND MORTALITY. Bier in his original article³ wrote: "Schleich's infiltration—and Oberst's regional—cocaine anæsthesia have restricted the dangers of general narcosis in a very essential and happy manner." Still for "large operations" both methods are available only to a slight extent. I have attempted to render large tracts of the body insensitive to pain by the cocainization of the spinal marrow. The indications, therefore, for spinal anæsthesia are for those larger operations in which local anæsthesia is unavailable, and in which general anæsthesia is contraindicated. The mortality of and the complications following general anæsthesia are sufficiently established for a fair comparison. Can we at this time compare it with the mortality and complication of spinal anæsthesia?

¹ New York Medical Journal, 1895, vol. lxii.

² Loc. cit.

³ Loc. cit.

MORTALITY OF SPINAL ANÆSTHESIA. Hahn¹ in his collective review finds recorded eight deaths among 1708 operations. These are not all the recorded deaths, but only those which might be attributed to spinal anæsthesia. If these figures are correct and further experience should corroborate them, the mortality of spinal anæsthesia will be greater than that of either ether or chloroform, and this method of anæsthesia would be distinctly contraindicated. Unfortunately the mortality of general anæsthesia is based upon all cases, and we have no careful estimate of the mortality of those cases suffering from pathological lesions, which, experience has taught us, increase to a great degree the danger of the anæsthetic. Many, perhaps the majority, of these 1708 cases of spinal anæsthesia suffered from these pathological lesions, and for this reason we are not yet able to estimate which is the safer anæsthetic, the general or the spinal, in this group of cases. So far no deaths have been reported following spinal anæsthesia in perfectly healthy individuals. At the same time we know the dangers of ether or chloroform are very slight in similar individuals. Hahn and others are inclined to believe that a number of cases of death following spinal anæsthesia have been concealed, and it does not seem unfair to conclude that in these "sub-rosa" cases no other cause outside of the spinal anæsthesia itself could be found. These cases seem to me sufficient to restrict the use of spinal anæsthesia to those patients in which we feel that a general anæsthetic has the greatest danger and in which local anæsthesia is impossible.

CASES OF DEATH FROM SPINAL ANÆSTHESIA REPORTED BY HAHN. Tuffier² has had at least five deaths in 252 operations. But Tuffier is of the opinion that in none should the spinal anæsthesia be considered the cause of death. Hahn states that in one which died on the day of operation (from asphyxia), and in which great changes in the heart and lungs were found at the autopsy, the operation might be considered the cause of death.

Dumont,³ in an experience with three cases of spinal anæsthesia, reports one death. The patient, a boy, seventeen years of age, died six days after operation, resection of the knee. The autopsy demonstrated general tuberculosis. Dumont feels that the cocaine was only an indirect factor, but seemed to hasten the death, and feels that a general anæsthetic would have been less dangerous. Dumont⁴ also mentions a case of Kocher's in which the patient, a boy, died a few days after an operation (resection of the ankle) with symptoms of meningitis.

Cavazzani, Foote, Lilienthal, and Draghescu, according to Hahn,

¹ Loc. cit.

² Matas, Philadelphia Medical Journal, November 3, 1900, vol. vi. p. 842.

³ Correspondenzblatt f. Schweizer Aerzte, October, 1900.

⁴ Loc. cit.

record each a death. The details are not given, and the original articles I have been unable to get.

Goilav¹ reports a case in a man, aged sixty-seven years.² The operation consisted in an amputation of the leg for arterio-sclerotic gangrene. The operation lasted forty minutes; toward the end and after the operation there were distinct symptoms of shock, later fever and delirium, collapse, coma, death in twenty hours—all symptoms of cocaine intoxication and apparently the cause of death. I believe that most surgeons will agree that a rapid operation under primary chloroform anæsthesia would have been distinctly safer in this instance. A second case of Goilav's also exhibited pronounced symptoms of cocaine intoxication, but recovered.

In America there are no reported cases of death among some 500 operations.³ The exact mortality of spinal anæsthesia is yet an unsettled question. The cause of death would appear to be a profound cocaine intoxication in patients weakened by certain pathological lesions. It seems impossible as yet to make any working comparison with the dangers of general anæsthetics. One conclusion, however, seems positive: spinal anæsthesia should never be performed in any case in which it is possible to execute the operation under local anæsthesia. So far in my own experience I have never been able to persuade myself to select spinal anæsthesia instead of general anæsthesia.

CONTRAINDICATIONS FOR SPINAL ANÆSTHESIA. Here opinions greatly differ, but a careful reading of the literature and the cases impresses one that the usual diseases in which in the past we have considered a general anæsthetic more dangerous are also more serious for spinal anæsthesia. It is in this group of cases that death has followed, and it is this group of cases in which the dangerous and uncomfortable post-operative symptoms of spinal anæsthesia are most common; therefore, so far in our experience it is simply a choice between two evils, and we are yet in the experimental stage in regard to judgment as to which is the worst. Most authorities agree that it should not be attempted in children under fifteen years, although there have been some successful cases. It seems contraindicated in all operations in which complete muscular relaxation is desired. It has, however, been attempted in all operations beneath the thorax. Of course, it has the same contraindication as local anæsthesia in regard to the mental condition of the patient.

There would be a great field for spinal anæsthesia if it could be

¹ Bull. et Mém. de la Soc. de Chir. de Bucharest, May 3, 1900.

² Review in the American Journal of the Medical Sciences, May, 1901, p. 596.

³ Murphy, Journal of the American Medical Association, February 9, 1901, vol. xxxvi. p. 359.

demonstrated that its effect on a diseased kidney is less than that of a general anæsthetic. The greatest obstacle to various surgical interventions for the relief of prostatic, bladder, and kidney affections is the danger of uræmia or anæmia following a general anæsthetic. The majority of authorities are of the opinion that spinal anæsthesia is safer, but I do not feel that there is yet sufficient evidence.

POST-OPERATIVE SYMPTOMS OF SPINAL ANÆSTHESIA. On the whole they are less common, of shorter duration and not as disagreeable as those after general anæsthesia, but it must be distinctly understood that there are very disagreeable secondary symptoms. Tuffier, who it must be remembered is an enthusiast, states that secondary symptoms are altogether absent in 20 per cent. of the cases. Other authorities observe that they are seldom absent, but there is simply a difference in their intensity. Nausea and vomiting are not uncommon (20 to 40 per cent. of cases). As a rule it lasts only a few hours. A most annoying symptom is headache, which may be very severe and last a number of days. Delirium is rarely observed, but in a few instances it has been quite marked. Dudley reports a case of mania twelve hours after operation. Disagreeable shooting pains in the lower limbs are not uncommon. Paralysis of the sphincter of the rectum and bladder have been observed. Symptoms of cocaine intoxication are almost always present; they may be very slight, in some cases very marked, and the patients are for some hours in a grave condition of collapse. As a rule the patients are more comfortable than after a general anæsthetic, but this should not influence one to choose spinal anæsthesia unless experience demonstrates that it is the safer method.

Later Post-operative Complications. So far there are no observations that the injection of cocaine into the subarachnoid space of the spinal cord produces any evil or permanent pathological changes. The clinical observations of patients observed some time after operation are negative, experiments on animals are negative, a few autopsies are also negative.

FAILURES IN SPINAL ANÆSTHESIA. It also must be remembered that a number of failures are on record; so that it may be necessary to give a general anæsthetic to complete the operation. This may be due to faulty technique, and in the future may be remedied. But as long as the possibility of a failure exists it adds discredit to the method. Murphy,¹ in his table of 631 cases—29 operators, reports 21 failures, 14 cases only partially successful, and 596 successful cases. Murphy is of the opinion that failure is due to faulty technique, and quotes Morton, of San Francisco, who was successful in his 31 cases. However, one operator (Racoviceanu) with an experience of 125 cases had four failures,

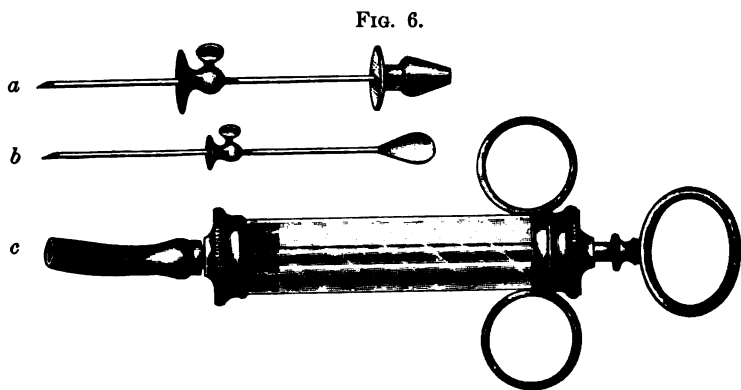
¹ Loc. cit.

Tuffier records no failures. There are, however, sufficient failures in the hands of experienced surgeons to demonstrate its possibility.

Another objection to spinal anæsthesia is its duration. It usually lasts about one hour, so that it is contraindicated for any operation of longer duration, and it would be a serious thing in instances where a short operation had required a longer time on account of some complication which might arise and which is not at all uncommon.

Richardson, of Boston,¹ has placed himself on record against spinal anæsthesia, and his description of Tuffier's cases which he witnessed in Paris does not agree very well with the publications of the latter.

THE TECHNIQUE OF SPINAL ANÆSTHESIA. Corning's description in 1888² differs somewhat from that used by later authorities. His needles and syringe are shown in Fig. 6. *b* is a fine needle, three



inches long, provided with a handle and a sliding nut. This needle is introduced half an inch laterally from the spinous process of the tenth dorsal vertebra until the bone is reached. The nut is then pushed down until it rests lightly upon the skin, and is secured in place by means of a screw. Fig. 7 shows this needle when it is withdrawn, and gives the exact distance between the skin and the cord. A hollow needle, Fig. 6 *a*, provided with a sliding nut fixed at the proper distance, is attached to a syringe, *c*, filled with cocaine solution. This hollow needle is thrust between the spinous processes of the tenth and eleventh dorsal vertebræ, and the syringe is emptied. Corning, in a later communication,³ gives a second description of his technique, which differs very little from the first, except that he has given up the first needle (Fig. 6 *a*) used for measurement and employs a delicate trocar containing

¹ Boston Medical and Surgical Journal, January 10, 1900.

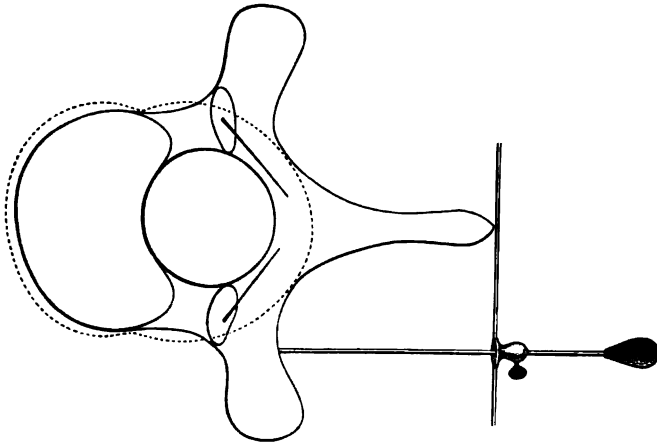
² Medical Record, 1888, vol. xxxiii. p. 291.

³ Ibid., October 20, 1900, p. 601.

a fine needle, and in making the injection uses the sitting rather than a lateral position. The needle should be introduced slowly, the appearance of a few drops of fluid indicates the penetration of the membrane when the syringe is attached and the injection made. The needle and the syringe are left in place until the anæsthesia is complete. (Fig. 8.)

Bier used Quincke's method of lumbar puncture with the patient in a lateral position and a thin hollow needle fitted with a stopper. After

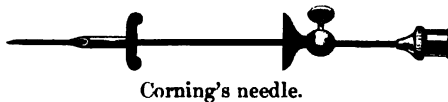
FIG. 7.



the appearance of the cerebro-spinal fluid the cocaine solution was introduced with a Pravaz syringe.

Matas,¹ after having experienced difficulty with Quincke's method, now follows that recommended by Tuffier,² but first used by Quincke: "The patient is seated on a table with his back to the operator. (Fig. 9.)

FIG. 8.



Corning's needle.

The hands resting on the thighs support the trunk. The lumbar region is thoroughly prepared with the usual antiseptic care. The trunk is held nearly upright, with the spine as straight as possible. The highest points of the iliac crests are now identified posteriorly (Fig. 10), a very difficult matter in obese patients, and a horizontal line connecting these two points is drawn across the spine. It will be found that the tip of the fourth lumbar spine touches this line. In

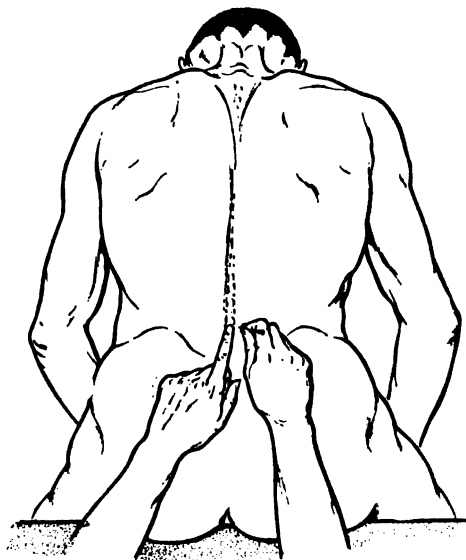
¹ Philadelphia Medical Journal, 1900, vol. vi. p. 838.

² Semaine Méd., May 15, 1900.

fat subjects it is often very difficult to identify the spine, and its situation can only be approximated. When it can be clearly identified, as in the majority of patients, it will usually be an easy matter to penetrate into the canal if the canula is thrust at a point just below and to the outer side of the junction of this line with the fourth spine. (Fig. 11.)

The skin at this point and for a quarter of an inch to the right of the median line is infiltrated with a few drops of Schleich's No. 1 or No. 2 cocaine solution.

FIG. 9.



The patient sits upon the edge of the table; the operator having previously localized the iliac crests, with the left index finger he locates the spinous process corresponding to the bi-iliac transverse line. The needle is inserted with the right hand 1 cm. in front of this apophysis. (TUFFIER.)

Murphy¹ follows Tuffier's method. Hahn in his collective review² writes: "The best developed method, because it has been tested on several hundred cases, is that of Tuffier. He uses a Pravaz syringe with a platinum needle 8 cm. long, lumen 6 mm. Fig. 12 represents the syringe and needles used by Tuffier."

Most authorities agree that the technique of lumbar puncture is sometimes a difficult one. In fat individuals and in very muscular subjects the palpation of the spinous process of the lumbar vertebræ is very difficult. The sitting position is better than the lateral. The needle should be introduced slowly, and the appearance of cerebro-spinal fluid

¹ Loc. cit.

² Loc. cit.

is the only indication that the membranes of the cord have been perforated, and the injection of the cocaine solution should never be done

FIG. 10.

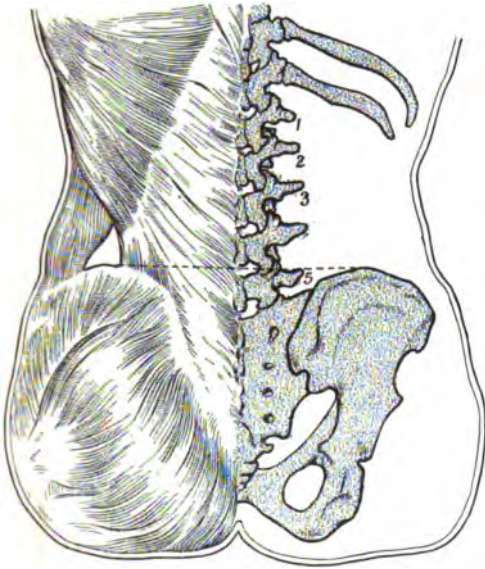


FIG. 11.

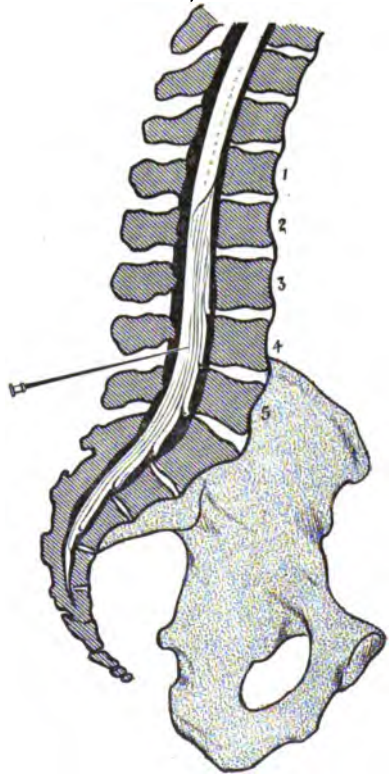
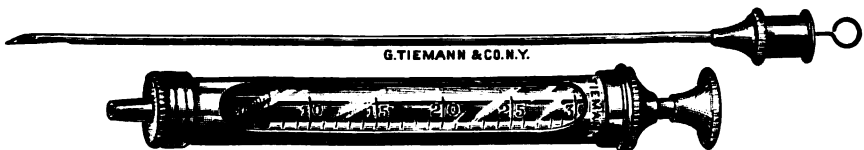


Fig. 10.—The broken line shows the vertebra corresponding in position to a horizontal line extending from the uppermost point of one iliac crest to that of the other posteriorly. (TUFFIER.)

Fig. 11.—The needle can be seen in the arachnoid space; the nerves being laterally situated are not in danger of injury. (TUFFIER.)

until this is observed. As little as possible of the spinal fluid should be allowed to escape. The cocaine solution should always be injected

FIG. 12.



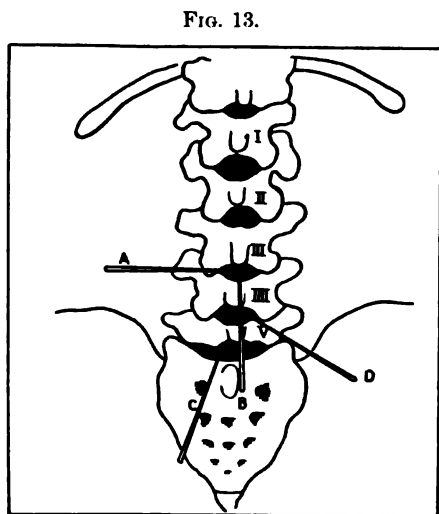
slowly, and at least one minute should be consumed in this procedure. After the injection the needle should be left in place for five or ten

minutes. Although repeated injections have been made when the first has failed or to prolong the anæsthesia, the majority of authorities agree that this adds to the danger of the method. It seems almost unnecessary to write that the most careful surgical cleanliness should be followed during the entire operation, and the solution of cocaine should be fresh and recently carefully sterilized. An infection would be a very serious and perhaps a fatal accident. So far none has been reported.

Corning, Bier, and other authorities anæsthetize the skin by Schleich's infiltration method or the ethyl-chloride spray previous to the introduction of the lumbar puncture needle. Tuffier and other authorities

think this is unnecessary, as the pain from the introduction of the puncture needle is very little, if any, more than that necessary to produce local anæsthesia after Schleich's method. One should have needles and syringes to be used exclusively for spinal anæsthesia, and they should be carefully tested previous to every operation.

THE POSITION OF THE LUMBAR PUNCTURE. A puncture through the intervertebral space, between the third and fourth or fourth and fifth lumbar vertebræ, has been universally selected as the preferable one. Chipault has used the space between the fifth lumbar vertebræ and the sacrum.



Method of puncture for spinal drainage. A. Quincke's method; B. Warfan's; C. Chipault's; D. Tuffier's—modified from Chipault.

Fig. 13, taken from Matas' article, well illustrates the different positions. Rodman also prefers Chipault's space. Corning originally introduced the needle between the eleventh and twelfth thoracic vertebræ, later between the second and third lumbar vertebræ, but now prefers the space between the fourth and fifth lumbar vertebræ. Tait and Cagliari, of San Francisco, have injected cocaine in the sixth cervical space. The majority of authorities, however, condemn an injection higher than the second lumbar vertebra.

THE PREPARATION AND THE DOSE OF THE COCAINE SOLUTION. The majority of authorities agree that the cocaine solution should be sterilized by the fractional method, although some authorities fear that heat destroys the action of cocaine. Experience with the local and general effect of sterilized solutions of cocaine in Schleich's method

gives no evidence for this conclusion. The majority of authorities use 1 cm. (15 minims) of a 2 per cent. solution of cocaine, as recommended by Tuffier. All authorities agree that a quantity of cocaine equal to 15 mgm. should never be exceeded. Matas gives the following excellent description of the preparation of the solution: "Five tablets, each containing $\frac{1}{2}$ grain of cocaine hydrochlorate, $\frac{1}{40}$ grain morphine hydrochlorate, $\frac{1}{2}$ grain sodium chloride, were dropped into 100 minims of hot distilled water and dissolved. The solution is again sterilized by the fractional method. Twenty minims of this solution represent $\frac{1}{2}$ of a grain of cocaine, $\frac{1}{40}$ of a grain of morphine, and $\frac{1}{2}$ of a grain of sodium chloride. The syringe, which contains 30 minims, is filled with the solution and 22 minims are injected; the excess of 2 minims is allowed for waste. The solution should always be used warm, about 90° to 100° F. The effects following the injection of this mixed cocaine-morphine-saline solution were so satisfactory that in future I shall continue to use this combination." Other drugs have been substituted for cocaine, eucaine B the most common, but as yet we have no evidence of their advantages over cocaine. Bier claims to have found a substitute, but has not yet published his results.

THE EXTENT OF THE ANALGESIA. Murphy¹ writes: "This first appears in from three to ten minutes after the injection, though it may be delayed to twenty or even thirty minutes. Sometimes it is preceded by a short period of hyperæsthesia involving different parts of the body. (Marx.) The analgesia almost always commences in the feet, but in rare instances is noted as a band around the body extending downward on the fronts of the thighs. Still more rarely the analgesia is ascending from the level of injection, involving the thorax, the upper extremities, neck, face, and occasionally reaching to the scalp. It can be estimated that the analgesia will be perfect up to the costal arch and will involve all of the abdominal viscera. Amputations of the breast have been performed without pain, but the upper limit of the analgesic area rarely extends high enough for the performance of this operation. The analgesia may be complete, partial, or entirely absent. Its duration is from 12 minutes to three hours, or even more. In one of Marx's cases it persisted five hours, but the average in our experience has been from twenty-seven minutes to one and one-half hours. During this period, particularly when the operation is a laparotomy, the tension of the muscles sometimes interferes with work, though not to a sufficient degree to seriously impede the continuance of the most difficult operation."

CONCLUSIONS WITH REGARD TO SPINAL ANÆSTHESIA. Hahn² in his collective review writes as follows: "It is possible and would be

¹ Loc. cit.

² Loc. cit.

very desirable indeed to find ways and means of modifying Bier's method so that it may satisfy the great expectations reposed in it. But it is of the most significance that a cool-headed and serious investigator like Bier himself, notwithstanding the great pessimism with which he judges his discovery in its recent form, still does not despair of a final beneficial result. He advises to think of means which would permit to render cocaine in the lumbar sac just as harmless as in other administrations, means which would prevent dangerous secondary symptoms, at the same time permitting an extension of the analgesia to the trunk and the upper extremities, and eventually to substitute for cocaine some other less toxic but just as effective agent. With such experiments Bier is occupied just now, and hopes to succeed in freeing the method discovered by him from its present defects. The drug which will be adapted to substitute cocaine he has found already, but he wishes to report on the results of his investigations only after the perfectly satisfactory completion of his experiments, which, presumably, may not be for some time. Accordingly we looked forward with a great deal of expectation to Bier's latest publication."

BIER'S LATEST COMMUNICATION ON SPINAL ANÆSTHESIA. The preceding critical review, based upon the literature and not upon my personal experience, because as yet I have never felt justified to perform spinal anæsthesia, was completed before Bier's latest article was published.¹ Bier's conclusions, from his own experience and from the literature, correspond so closely with mine that one who reads both might easily believe that my critical review was based on Bier's article. It is therefore unnecessary to repeat Bier's criticism of his own method. In conclusion he writes: "For this reason I draw no other conclusion from the large number of 1200 operations performed under cocaine anæsthesia of the spinal marrow, in the form first described by me, than that arrived at from my first observation, namely, that the method in its present form is unfit for general employment."

Corning,² in an article entitled "Some Conservative Jottings Apropos of Spinal Anæsthesia," like Hahn, cautions us against the new method, and writes: "Again, I repeat, I am no surgeon, but as a neurologist I tremble for the cord."

Spinal anæsthesia, it must be remembered, has its mortality. The technique of lumbar puncture in certain individuals has been found to be difficult, in some cases on account of complete or partial failure to produce analgesia it has been necessary to resort to a general anæsthetic to complete the operation. The average time of the anæsthesia

¹ *Archiv f. klin. Chir.*, 1901, Band liv. Heft 1, 236.

² *Medical Record*, October, 1900.

is short and often uncertain ; disagreeable, sometimes serious post-operative symptoms have been observed. This method of anæsthesia is, therefore, in its experimental stage, and should be resorted to only after the most careful deliberation in certain selected cases.

Bier has attempted to remedy the defects in his method by numerous experiments on animals made by his assistant, Dr. Eden :

1. To replace cocaine by kindred but less toxic anæsthetics or totally non-toxic substances. So far they have found that eucaïne B is a slight improvement on cocaine.

2. To administer the respective toxins in sufficient quantities, but greater dilutions, into the spinal canal.

3. To find a method for limiting the toxic effects of the anæsthetic as much as possible to the spinal marrow, and to keep it from the brain, because the entire character of the discomforts and the dangers described as due to cocaine point to their origin in the brain and the extended marrow.

Believing that the diffusion of the intraspinal drug is through the cerebro-spinal fluid rather than through the circulation, Bier has attempted to restrict the flow of the spinal fluid into the meningeal spaces of the brain by elastic ligature around the neck ; this, of course, produces venous obstruction and increases the amount of blood in the brain, and consequently, it is reasoned, the flow of the spinal fluid into the cerebrum is checked. Even if this is correct theoretically, practically in man, even admitted by Bier, the elastic obstruction is somewhat difficult in all cases, and may become dangerous in patients with marked arteriosclerosis.

In spite of the change in the method Bier freely admits that it is in its experimental stage.

OPERATIVE TECHNIQUE AND WOUND TREATMENT.

On this subject there is still much division of opinion, and many problems are by no means settled. Clinical experience is frequently at variance with the apparent results of experimental investigations.

The Treatment of Recent Wounds, such as Compound Fractures, Etc. The question whether recent wounds shall be treated with aseptic or antiseptic irrigation is still a mooted one. Experimental investigation appears to show that it is impossible to disinfect completely a recent wound made in animals and immediately infected with some micro-organism. Schimmelbusch is the chief exponent of this doctrine, and he believes that the necrosis of the tissues due to the irritation of the antiseptic irrigation is more harmful than the good derived from the

partial destruction of micro-organism by the antiseptic, and believes that irrigation with boiled water or salt solution is just as efficacious as with antiseptic solutions. Clinical experience, on the other hand, would seem to indicate that better results are obtained in the treatment of recent open wounds by proper antiseptic treatment. One who has read Lister's early work cannot but be impressed profoundly with the almost marvellous differences in the results in the treatment of wounds, especially compound fractures, simply by the antiseptic use of carbolic acid. Here, with absolutely no asepsis and with only antiseptics, astonishingly good results were obtained, even in most unsanitary environments. That antiseptics is now unnecessary, even when surrounded with perfect asepsis, can hardly be believed. Recent wounds are, probably without much doubt, always infected to a more or less degree. We can easily believe on the one hand that the number and virulence of the micro-organisms are so slight that the wound would heal without evidence of infection, whether it is washed out with sterile or antiseptic solution, or not; on the other hand, experimental investigation and clinical experience clearly demonstrate that if the wound is infected with an organism or organisms of great virulence it is impossible to disinfect in every instance such a wound. So that the infection of recent wounds when properly treated with disinfectants is not the fault of the method, but due to the unusual virulence of the micro-organism. Such infected wounds would surely not have been any less infected, or their subsequent course any less serious, if only sterile irrigations had been used, and it is an open question whether the number of such infections is not very much reduced by their proper antiseptic treatment in their recent state. When we group all wounds, including these two extreme groups just mentioned, clinical experience, it appears to me, is almost overwhelmingly in favor of the treatment of recent wounds with antiseptic irrigations.

Bacteriological Investigation of Recent Accidental Wounds. On this subject there has been very little investigation. Like Schimmelbusch, most investigators confined their studies to wounds made in animals which they infected with pure cultures of the various pyogenic bacteria, and then studied the effect of the antiseptic and aseptic treatment. That they were able to demonstrate that the antiseptic irrigation of the wound, almost immediately or at various intervals after the introduction of the bacteria, did not prevent the entrance of such germs into the circulation of the animal, nor completely destroy them in the wound, does not, in my judgment and that of many others, prove the ineffectiveness of the antiseptic treatment of recent accidental wounds met with in surgical practice.

The conditions met with in recent accidental wounds are entirely

different from those artificially created in these experimental studies. The pyogenic germs are seldom, if ever, introduced in such numbers and of such virulence. The demonstration of bacteria in the circulation after the antiseptic treatment of experimental wounds is a fact of little importance. In accidental wounds it is the rarest occurrence to have symptoms of general infection until sometime after the signs of local infection, and without doubt in these cases the general infection is due not to the bacteria first introduced in the recent wound, but to their descendants, which have multiplied and gained in virulence by growth in the tissues of the recent wound. Also the demonstration that bacteria are still present after the antiseptic treatment of the experimental wound is no proof that such treatment has not only not reduced their numbers but also their powers of doing harm. Nor does it prove that the danger of subsequent infection from such bacteria is not lessened by the antiseptic treatment.

Granting the value of these laboratory investigations it seems pretty well settled that the question must be solved by the bacteriological study of recent accidental wounds and the observation of the course of such wounds treated aseptically or antiseptically. As I stated before, clinical experience based upon the observation of recent accidental wounds treated by both methods favors antiseptics. That the present method of antiseptics in recent accidental wounds does not prevent the growth of the bacteria first introduced and their results—local infection—in a certain percentage of cases must be admitted. In such instances it seems pretty clearly settled that the bacteria introduced are in unusually great numbers and virulence. The problem of the complete disinfection of the wound in such cases is not yet settled.

Voluminous as the literature on surgical bacteriology is in general, that on bacteriological investigation of recent accidental wounds is very meagre. Riggenbach, writing on this subject from the surgical clinic of Prof. Haegler in Basel,¹ states that after a most careful search of the literature he can find very few investigations on this subject. Riggenbach's work is most thorough, and will stand, no doubt, as not only one of the first, but one of the best in this field. He started out to make careful bacteriological examination of every recent accidental wound, noting first the duration of the time between the receipt of the injury and the time of the first bacteriological examination. In addition to ascertaining by cover-slips and cultures the variety or varieties of bacteria in the recent wound, their pathogenesis was estimated by animal investigation. The ultimate healing of each case was carefully observed after the different methods of treatment, and subsequent bacteriological

¹ Deutsch. Zeitschrift f. Chir., Band xlvii., 1898, p. 33.

examinations were made of the secretions from each wound. Riggensbach soon found that each case took so much time that he allowed himself to be content with twenty-four observations. The interval of time varied from thirty minutes to three days. Eight wounds were incised, sixteen lacerated. In every wound the cultures showed the presence of bacteria, and in only one case were these organisms not pathogenic. In the majority of instances two or more varieties were found. In fifteen cases, or 62.5 per cent., the *staphylococcus pyogenes albus* was present. The *streptococcus pyogenes* was found in eleven cases, or almost 50 per cent. The tetanus bacillus was found in two cases confirmed by animal inoculation. In one the wound had been contaminated by earth. Both wounds were thoroughly disinfected. In one case, in which the tetanus bacillus was associated with *streptococcus pyogenes* and other bacteria, the wound of the finger was of one hour duration; it was closed with sutures and healed per primam. In the other the tetanus bacillus was associated with the *staphylococcus pyogenes aureus*, *streptococcus*, and other bacteria. It was a lacerated wound of the ball of the thumb of six and one-half hours' duration; the patient had washed the wound in river-water, sutured it with common thread, and covered it with a piece of cotton wet with carbolic acid solution. Riggensbach opened the wound, and after disinfection left it open. The wound healed by granulation without any evidence of infection. In four cases the *micrococcus tetragenus* was found. The *staphylococcus pyogenes aureus* was found in eight cases. But one of the twenty-three was a pure infection, and that with the *staphylococcus pyogenes albus*. In this case the wound of forty-four hours was lacerated and confined to the end of the finger; it was disinfected, left open, and healed without infection. The culture from the wound killed a rabbit in six days; there was a local abscess at the point of injection, with multiple metastatic abscesses, cultures from which demonstrated a pure infection with the *albus*. In only three out of the twenty-three cases *staphylococci albus* or *aureus*, or the *streptococcus*, were not found, but other less common pyogenic cocci and bacilli. These interesting observations demonstrate the frequency of the introduction of pyogenic bacteria in recent wounds. That almost 50 per cent. contained *streptococci*, and that two contained the bacillus of tetanus, is an observation hardly to be expected.

It is not necessary to go into details, but Riggensbach concludes that even in these twenty-four cases the wounds treated by the antiseptic method, whether closed or open, healed better than those treated by the aseptic method, and in addition he was able to demonstrate that the continuous antiseptic treatment of the wounds left open to heal by granulation diminished the number and virulence of the bacteria, and

when the dressings were changed to the aseptic the number of bacteria increased after about forty-eight hours. Riggenbach's conclusions make him favorable to the antiseptic treatment of recent accident wounds. Henle,¹ Messner,² and Schanjawski,³ from their clinical and experimental studies, come to the same conclusions as Riggenbach.

Riggenbach's observations on the *staphylococcus pyogenes albus* are of great interest. The demonstration that this pus coccus was present in 62.5 per cent. of the cases clearly indicates that the skin of the patient is the most common source for the infection of recent wounds. That this germ is the normal inhabitant of the human skin is now well known, since the demonstration of Welch and others, that it can be pathogenic in both man and animals, is clearly demonstrated in Riggenbach's studies in confirmation of many other authorities. Riggenbach also confirms the interesting observation of Bertoyi,⁴ who succeeded in getting the aureus from continuous cultures of the albus. Riggenbach admits the possibility of contamination. Quite a number of recent bacteriologists are inclined to the view that the aureus may be cultivated in successive generations from the albus, and that it is but a more virulent variety of the same micrococcus. Certain observations indicate the truth of this view, for example, after the most careful mechanical and chemical cleaning of the skin we can usually demonstrate in cultures, by using a piece of skin or passing a silk thread through the skin, the presence of the *staphylococcus pyogenes albus*; yet when such wounds suppurate the cultures from the purulent material rarely show pure albus, but both white and yellow colonies, and it seems but natural to infer that the infection of the wound took place from cocci already present in the skin, and these albus cocci, on account of the better conditions for growth in the secretion of the wound and by successive generations acquire a greater virulence, and when later transplanted to the artificial media, assume both the white and yellow color.

Clinical observations and experimental investigation on the value of the antiseptic treatment of infections and infected wounds, if favorable to the antiseptic treatment, can be used as an argument in favor of the disinfection of recent accidental wounds, because there are sufficient observations to clearly prove that recent accidental wounds should be considered infected wounds, although the macroscopical evidence of the presence of such pyogenic bacteria is not yet manifest. In the section on the treatment of infections and infected wounds it will be

¹ Centralblatt f. Chir., Supplement to No. 30, 1894; and Archiv f. klin. Chir., 1895, Band xlix.

² Centralblatt f. Chir., Supplement to No. 30, 1894, and Münchener med. Wochenschrift, 1894, No. 19.

³ Wojenno-medicinski Journal, 1896.

⁴ Lancet, 1886, vol. i. No. 7.

seen that recent literature is distinctly favorable to the antiseptic treatment.

Conclusions as to Treatment of Recent Wounds, such as Compound Fractures, Etc. We must bear in mind, first, that every recent wound is infected with bacteria of varying numbers and virulence. On the one hand the virulence of the infecting germ may be of such a high degree that no matter how slight the destruction of the tissues by the injury, nor how carefully it is disinfected, even at a short interval after the injury, wound infection will take place. If we could recognize such a virulent infection, the wound should not only be disinfected, but should be left wide open, the two most important factors in the treatment of a grave infection. On the other hand, the destruction of the tissues by the injury may be so extensive that no matter how few the number of germs, nor how low their degree of virulence, infection of the wound may follow, because the necrotic tissue makes such an excellent culture medium and because the circulation of the tissues is enfeebled and resistance lower. No surgeon would think of closing such a wound, and clinical experience clearly demonstrates that the antiseptic treatment aids in combating and limiting the infection. It not only acts upon the bacteria already in the wound, but far better than the aseptic method lessens the possibility of secondary infection. The first possibility—a very virulent infection—we cannot always anticipate, so that when a recent wound in which all the injured tissues have good circulation, and which, after proper disinfection, we have closed, shows signs of a virulent infection we must not blame ourselves nor the method, but promptly conclude that the bacteria introduced at the time of the injury were of unusual virulence, and promptly and energetically treat the wound infection on that supposition. Sometimes we can feel quite positive that the infection of the recent wound is a virulent one, for example, injuries received during autopsies or operations on cases in which we know the nature of the infection, injuries with instruments which we know were probably infected, recent wounds which, from the history of the evidence on the wound itself, show contamination with earth. In such instances the wounds should not only be more energetically disinfected (with pure carbolic acid, as will be discussed later), but should be left open for further disinfection; if the original skin incision is smaller than the subcutaneous wound it should be enlarged. The second possibility (the extensive destruction of the tissues) is always an indication, not only for thorough disinfection, but for larger skin incisions, if necessary, and for the open-wound treatment. The time between the injury and the first treatment is a third and very important factor to indicate the method of treatment. The longer the interval the greater the opportunities for infection, for during this time the bac-

teria have had opportunity not only to grow, but to penetrate beneath the surface of the wound, a position difficult to reach with disinfectants. The increased interval of time therefore influences us, irrespective of the other factors, to treat the wound by the open method.

The Treatment of Infected Wounds. Schimmelbusch and his followers who, fortunately only for a short time, made aseptic surgery popular (almost a fad), are responsible for many disastrous results. Fortunately, many surgeons like Halsted never accepted aseptic surgery, except in an extremely limited field, and certainly never in the treatment of recent or infected wounds. In the literature of the last few years the pendulum has swung. Not only clinically, but even the results of animal experiments do not confirm the work of Schimmelbusch and his followers. Riggenbach¹ in the discussion of the literature brings out this fact. Later Carl v. Eicken,² writing from the clinic of Prof. Czerny in Heidelberg, confirms the view of Riggenbach not only from the clinical observations and animal experiments of others, but from his own. It does not seem necessary to go into details of the animal experiments which deal with wounds infected with the most virulent pyogenic organisms treated experimentally by various methods, but with the conclusion that the antiseptic method is far better than the aseptic in conjunction with other measures in the treatment of infected wounds and infections. As to the other measures, free incisions, wide open wounds, frequent irrigation, and moist rather than dry dressing, and frequent changing of the dressing, there is very little if any disagreement among surgeons.

Pure Carbolic Acid in Infected Wounds and Infections. Although the majority of surgeons favor the antiseptic treatment of infected wounds and infections, no one is by any means content that the method gives ideal results, nor have they felt that it has reached its limit of usefulness. The common antiseptic solutions used, bichloride of mercury and carbolic acid, have their danger, systemic poisoning. This danger unquestionably is greater with the carbolic acid solution. In addition, the continuous application of dressings wet with solutions of carbolic acid may produce gangrene. For this reason solutions of mercurial sublimate have been more commonly used, but even with this we are restricted in its use not only as an irrigation but for a continuous wet dressing on account of the dangers of absorption and poisoning. What we need is an antiseptic of great power which can be applied directly to the tissues and without danger of systemic poisoning or local necrosis of any great extent.

The recent literature on carbolic acid shows to a rather large extent

¹ Loc. cit.

² Beiträge zur klin. Chir., 1899, vol. xxiv. p. 353.

an apparent ignorance of the history of antiseptic surgery. Many seem to forget that Lister's first work was done with pure carbolic acid, and he clearly demonstrated, without the shadow of a doubt, that both large surfaces of recent injuries and large surfaces of infected tissues could be swabbed with pure carbolic acid without danger of systemic poisoning, and that the amount of local necrosis was not sufficient to interfere with the healing. Every student should read Lister's first publication, which appeared March 16, 1867,¹ on "A New Method of Treatment of Compound Fractures, Abscesses, etc., with Observations on the Condition of Suppuration." In these cases of compound fracture Lister introduced through the wound in the skin a cotton swab saturated with pure carbolic acid one or more times, thoroughly wiping the surface of the wound with this swab. The opening in the skin was allowed to fill with the blood-clot saturated with carbolic acid; over this was placed a piece of cloth saturated with the same pure carbolic acid. In these papers Lister carefully describes the healing under this scab and the organization of the blood-clot, a method of wound treatment and healing later so extensively used and advocated by Schede. From Lister's work the value and the possibility of pure carbolic acid in the treatment of wounds and infection are fully demonstrated. Lister soon found that the dressing wet with pure carbolic acid excoriated the skin, and for this reason he began to use dilute solutions. This change was made because of the local action of the strong acid, not because of any systemic poisoning. It was with the dilute solutions of carbolic acid that Lister fully developed the technique of antiseptic surgery. Coincident with the general adoption of this method and the use of the spray, cases of carbolic acid poisoning were observed, many fatal. In 1875 Billroth began to use Lister's method, and writes (*Clinical Surgery*): "In short, in every detail, to the best of my power, I carried out Lister's and Volkmann's instructions. For a time matters went on better, but then cases of carbolic poisoning and carbolic eczema became so common that I gave up this antiseptic, replacing it by thymol." In conclusion Billroth writes: "In former times the surgeon felt that he could do something himself for operation cases by careful watching and supervision; but nowadays so much depends upon the hands and clothes of assistants and nurses, and on the intelligence of the workmen who manufacture the dressings, that the surgeon, though answerable for the fate of his patients, often has not the circumstances wholly under his control. The proper management of cases under the antiseptic system is the most difficult task that I have ever attempted; still, this shall not prevent me from doing my very best to perfect the system." A

¹ Lancet, 1867, vol. i. p. 326.

careful reading of Lister's publications gives one the impression that the founder of antiseptic surgery experienced very few serious or disastrous results from the systemic poisoning of the carbolic acid solutions. In 1883¹ Lister wrote that he had given up the spray. That Lister had some fears of carbolic acid poisoning can be inferred from the fact that in 1884 he introduced corrosive sublimate as a substitute for carbolic acid solutions in wet surgical dressings. He states that his attention to the antiseptic value of corrosive sublimate was due to the work of Koch in 1883-1884. As far as I can ascertain, Lister never returned to his original use of pure carbolic acid.

That pure carbolic acid has been employed by many surgeons up to the present time, similar to the original method of Lister, I am quite certain, especially in the treatment of infected wounds and infections. This is certainly true in Prof. Halsted's clinic, where the antiseptic treatment of wounds has been constantly employed in its proper place. It is our rule to swab with pure carbolic acid the exposed surfaces of infections and infected wounds, frequently using quite large quantities of the pure acid. Especially in treatment of the bone cavity after operations for osteomyelitis has Halsted used pure carbolic acid.² We always use pure carbolic acid as the chief disinfectant in operations for tuberculosis of the joints, particularly when a complete excision is not performed.³ Dr. Halsted has frequently told me that in his early treatment of acute purulent arthritis due to pyogenic cocci or the gonococcus, he swabbed the entire joint cavity out with pure carbolic acid, but later observations demonstrated that in irrigation of a joint with 1 : 1000 bichloride was a disinfectant of sufficient strength in these cases, and that the danger of ankylosis seemed much less when the weaker antiseptic was used.⁴

Following the suggestions of Dr. Halsted, I have used pure carbolic acid in his clinic very extensively, and the last few years, on account of the excellent results, more extensively. Not infrequently I have swabbed fresh accidental wounds with pure carbolic acid, chiefly in those cases in which I felt the possibility of virulent infection to be greater than usual.⁵

I am induced to make this preliminary statement because I feel, as stated before, that many surgeons still use pure carbolic acid similar to

¹ *Lancet*, 1883, vol. lxxx. p. 220, No. 2.

² *Treatment of Wounds*, Johns Hopkins Hospital Reports, 1891, vol. ii. p. 293.

³ Bloodgood. *Early Exploratory Operations for Tuberculosis of the Hip*, Johns Hopkins Hospital Bulletin, January, 1900, No. 106.

⁴ See *Incision and Irrigation of Joints for Gonorrhœal Arthritis*, Johns Hopkins Hospital Reports, 1891, vol. ii. p. 289.

⁵ *PROGRESSIVE MEDICINE*, December, 1899, p. 170

the original method of Lister, although in recent literature one finds little on this subject.

A recent article by A. M. Phelps, of New York,¹ read before the Third International Medical Congress, in Paris, 1898, seems to have revived the general interest in the use of carbolic acid. Phelps, in advocating the earlier exploration of tubercular and other suppurating conditions of the joints, details his most satisfactory experience with the disinfection of the infected cavities by pure carbolic acid. Phelps finds the field of pure carbolic acid greatly increased by the recent knowledge of the antidotal effect of alcohol to pure carbolic acid. According to Phelps, this was first demonstrated by Dr. S. D. Powell, of New York, who had used carbolic acid for years in the treatment of various infections.² That alcohol renders carbolic acid inert has been known for a long time. I referred to this in *PROGRESSIVE MEDICINE* for December, 1899 (p. 157), in a discussion of an article by Senger. The practical application, however, of the use of absolute alcohol and pure carbolic seems to have been introduced by Powell and Phelps. It is as follows: Previous to the introduction of carbolic acid into the wound the skin about the edges of the wound is moistened with a sponge saturated with absolute alcohol. This precaution renders inert and prevents excoriation of the skin by any of the pure carbolic acid which might accidentally come in contact with the skin. Should any pure carbolic acid fall upon the skin not so protected, its corrosive action can be prevented by immediately sponging the spot with 95 per cent. or absolute alcohol. The pure carbolic acid can be introduced into the wound by means of a saturated swab, or, according to Phelps, the cavity can be filled with pure carbolic acid; the acid is allowed to remain one minute by the watch; the cavity is then thoroughly washed out with pure alcohol, and the alcohol washed away with a 2 per cent. solution of carbolic acid. When the cavity is simply swabbed with the carbolic acid it is then only necessary to use a similar swab of absolute alcohol. I found this suggestion of Powell and Phelps of the greatest value, and it has greatly increased the field of usefulness of pure carbolic acid. Phelps in his most energetic use of pure carbolic acid has, similarly to previous observers, never seen a case of systemic poisoning, nor any bad local effects. He believes that the acid penetrates some distance in the tissues and destroys bacteria as far as it penetrates. My own experience agrees with that of Phelps, that the disinfection with pure carbolic acid is much more efficacious than any yet known method.

¹ New York Medical Journal, 1900, vol. lxxii. p. 366.

² No reference to Dr. Powell's work is given by Dr. Phelps, and I have been unable to find the original.

Prof. von Bruns and his assistant, Honsell¹ have recently published their experience with carbolic acid. In the first part, von Bruns writes concerning the practical value of pure carbolic acid in septic wounds and suppurative processes, speaking of it as Phelps' method, and states that he has used it in more than eighty cases, including joint suppurations. Not more than 2 to 6 grammes of pure carbolic acid is used in any one case. The method of application employed by von Bruns does not differ at all from that first employed by Lister, and he writes in conclusion: "It might be called a dispensation of Providence if that remedy which has started the entire antiseptic area, and has since then been generally discarded, were destined to serve us again in our war against wound infection."

In Part II., by Honsell,² is an experimental investigation instituted to clear up some points with regard to the safety and character of the action of Phelps' method. In animals quite large subcutaneous injections of pure carbolic acid seldom produce death, while a similar amount of the diluted acid killed the animal within an hour. With the pure solution there is at once a formation of a corrosive eschar, and the majority of acid remains unabsorbed while the diluted solutions are quickly absorbed. We know from Lewis and others that 2 to 6 grammes of pure carbolic acid may be injected in the hydrocele sac without any danger of local or general deleterious effect. Clinically the subcutaneous injection of pure carbolic acid for infections has on the whole not yielded especially good results. It is not uncommon that the eschar later acts as a foreign body and an abscess forms. Honsell's experiments with pure carbolic acid in the disinfection of open wounds has demonstrated that the pure acid is much less toxic than the dilute. It may be used up to 6 grammes without danger if after the duration of about one minute the surfaces are irrigated with alcohol. The chief value of the alcohol is that it takes up the excess of carbolic acid and protects the skin from its excessive corrosive effect. The germicidal action of pure carbolic acid is not affected by the tissues and their juices. Experimentally it destroys the *staphylococcus pyogenes aureus* in one minute, while 3 per cent. carbolic acid takes from five to fifteen minutes and 1:1000 bichloride longer. The pure carbolic acid also seems to have a slightly continuous germicidal effect. In addition, its corrosive action produces in the tissues a certain amount of reaction which aids in the localization and the limitation of the infection. It unquestionably aids and hastens the separation of the necrotic tissue produced by the infection. These experimental investigations of Honsell simply con-

¹ Archiv f. klin. Chir. 1901, Band lxiv. Heft 1, p. 198.

² The complete article is in Beiträge zur klin. Chir., 1901, Band xxx. Heft 2, p. 328.

firm that which we have known for years from clinical experience. The addition of alcohol is, however, an important point in the technique. As Honsell states, alcohol is not a true antidote for carbolic acid, it simply acts better than water in absorbing carbolic acid in removing the excess of the acid from the wound and preventing an excessive corrosive action.

Kehrer¹ has used pure carbolic acid in the disinfection of the infected uterine cavity and vagina since 1889, and during twelve years has never observed any toxic effect. Maylard² has used pure carbolic acid extensively in the treatment of gangrenous inflammations. Dr. F. Pirkner³ discusses the use of alcohol in the treatment of carbolic acid burns and poisoning. Pirkner believes that carbolic acid acts as an antidote, that is, when carbolic acid is taken by mouth, alcohol if given a short time later will not only inhibit its corrosive action on the mucous membrane, but will neutralize the toxic action of that already absorbed in the blood. Honsell from his experiments has demonstrated that this is not so. Wood in his text-book simply refers to the publication of Phelps and Fraser. In case of carbolic acid poisoning one should depend on alcohol only for its neutralizing power, and the soluble sulphates should be given to act as the antidote for the acid already in the circulation.

This recent revival of the use of pure carbolic acid in antiseptic surgery is only another demonstration that there is still much work to be done in perfecting our treatment of infections and infected wounds. No check should be allowed in this investigation until true antitoxin sera have been discovered for the different infections.

Hand Disinfection. The literature of the past two years is unusually voluminous in experimental and clinical studies with regard to hand disinfection and of gloves. It may be summarized as follows: Surgeons and nurses should avoid in every way allowing their hands to come in contact with any wound or material containing virulent bacteria. This is best accomplished by wearing gloves in all operations for infections; in dressing all infected or suppurating wounds either gloves should be worn or the entire dressing should be performed with instruments. The latter procedure protects not only the surgeon from infecting his hands with the discharges from the wound but also protects patients with uninfected wounds from danger of infection from the surgeon's hands. That there is a general neglect on the part of many surgeons and nurses in regard to the infection of their own hands in the handling even of virulent infected cases cannot be denied. That infections at the operat-

¹ Müller's Handbuch der Geburtshilfe, Band iii.

² British Medical Journal, 1897, p. 1475.

³ American Medicine, May 25, 1901, p. 358.

ing-table and the secondary infection of clean wounds after operation from direct contact with infected hands not infrequently take place must be admitted.

In the disinfection of the hands the best results are obtained from a combination of mechanical and chemical methods. Even when gloves are worn the same care should be taken in the cleansing of the surgeon's hands. Haegler has recently published a book of 210 pages entirely devoted to hand disinfection. With experience of twelve years, both clinical and experimental,¹ Haegler advises that it is most important to prevent even the slightest injury to the hands, because in these even most minute wounds virulent bacteria grow, and it is almost impossible to disinfect. The surgeon should take the greatest care of the skin about the nails, the part of the hand most difficult to disinfect. I have found since I have worn rubber gloves as a routine that the condition of the epidermis of my hands has been uniformly better. In the thorough disinfection of the hands previous to all operations the technique remains unchanged, but previous to the use of gloves it was constantly necessary to rinse the hands in bichloride during the operation, not only to wash off the blood, but to redisinfect because of the accidental touching of the skin of the patient or some other much less cleanly thing during the operation. This frequent immersion in bichloride, combined with the soiling and rubbing in of blood during the operation, always rendered the epidermis, especially around the nails, rough and not infrequently slightly excoriated, so that the next disinfection of the hands was more difficult. This irritated condition would not infrequently compel someone to rest from operations for a number of days. Since the introduction of gloves I have observed that this rarely happened. In the wards at the surgical dressings we have given up any attempt at chemical disinfection; the hands are simply washed with soap and water. Ordinary wounds are dressed with instruments. If we wish to be especially clean, gloves are worn. If the case is an especially infected one we also wear gloves. This method unquestionably aids in keeping the surgeon's hands in much better condition. I mention this in confirmation of Haegler's statement that one of the most important points in the technique is to keep the skin of the hands in good condition. A number of surgeons have given up bichloride and other chemical disinfectants because of its action on the epidermis. My own experience teaches that the fault is not so much the chemical disinfection itself, but the way in which it is accomplished. Haegler further writes that if we wish to sterilize our hands as perfectly as possible, chemical disinfection cannot be given up. In addition to the most painstaking mechanical, scrubbing, paring, and

¹ Review, *Centralblatt f. Chir.*, 1900, Band xxvii. p. 1151.

cleaning of the nails, we must use a combination of strong chemical antiseptics before allowing the naked or gloved hand to be introduced into a wound. Haegler voices the opinion of the majority of experienced and careful surgeons when he writes that the chemical disinfection of the skin cannot and should not be given up. Ether and alcohol are by no means sufficient; we must use in addition at least 1 : 1000 bichloride. In the Surgical and Gynecological Clinics of the Johns Hopkins Hospital we have found no reason to give up the additional use of permanganate of potash and oxalic acid, in addition to alcohol, ether and bichloride, in the disinfection of the hands of the surgeon and the skin of the patient.

It seems hardly necessary to discuss any more of recent literature than that of Haegler. No method has yet been found which will render absolutely sterile the skin, but the clinical and experimental evidence is all in favor that we must use chemical disinfection, and that if possible the surgeon should wear gloves, and that rubber gloves are distinctly better than cotton gloves. It also must be borne in mind that it is almost impossible to completely disinfect the deep follicles of the skin. Fortunately, in the majority of instances, only the staphylococcus pyogenes albus is found in this situation, but it must be remembered that in some instances the skin of the patient may contain a very virulent micro-organism. This may explain some of the cases of streptococcus infection following operation in which every other avenue of infection but this could be excluded. We need further bacteriological studies of the disinfected skin to definitely prove this possibility.

Asepsis and Antisepsis. The correct adjustment of these two methods is fast approaching. As antisepsis in the early days of surgery was a necessity, later asepsis became almost a fad. Until we have accomplished the perfect disinfection of the skin, asepsis is impossible. At the present time everything but the hands of the surgeon and the skin of the patient can be rendered absolutely sterile; in addition the hands can be almost excluded by the use of rubber gloves, but during the operation the exposed surface of the skin around the region of the wound can still be a source of slight infection to everything that comes in contact with it. In addition, it must always be remembered that there is a possibility during the operation that the hands, instruments, sponges, ligatures, and so forth, come in contact with something not surgically clean. This is especially true in all large surgical clinics in which, at not infrequent intervals, inexperienced assistants and nurses assist at the operation, so that in every clean operation, even with the very best technique, there is always the possibility of more or less infection of the wound, and the question naturally arises: shall we use any antiseptics during clean operations? This is one of the most difficult

questions to answer. As stated in the previous section, the majority of authorities now favor antisepsis in recent accidental wounds and infected wounds. Granting, therefore, that the wound at any operation may be slightly infected, does it not seem fair to conclude that a certain amount of antisepsis will not only aid in the prevention of such infection, but will lessen the dangers of the infection when it does take place. Bumm¹ has bacteriologically examined the entire aseptic operation apparatus of the clinic in Basel in order to ascertain which method warrants a more certain absence of germs, the aseptic or the antiseptic. The former proved entirely insufficient. Already at the beginning of the operation there were germs on the hands, tampons, in the wound, ligating material, and in the "sterile" salt solution, which gradually increased. He found the most varying species of bacteria, especially the staphylococcus albus and aureus, less frequently streptococci. The hands always proved the place where they came from. The disinfectants now at our service are therefore insufficient, and so is alcohol, which only hardens the skin, and leaves the germs in the depth unaffected. After these experiences Bumm has returned again to antisepsis, which gives better bacteriological results than asepsis.

The practical results of aseptic surgery, especially when combined with the use of rubber gloves, are, on the whole, excellent; but this bacteriological study of Bumm and clinical experience demonstrate the possibility of infections and now and then virulent infections. Gottstein, writing from Mikulicz's clinic² on observations and experiences on asepsis, states that during the last two years in this clinic there had been a sufficient number of infections during asepsis to stimulate them to investigate the cause, with the conclusion (not at all a new one) that the fault lay with the disinfection of the hands of the surgeon and the skin of the patient.

In view of the evident facts that perfect asepsis is yet impossible in the disinfection of the skin, and in view of the possibility that during clean operations infections may take place, would it not be safer to use a certain amount of antisepsis? At the present time this is a question which each surgeon in charge of a large clinic must decide for himself, based on the experience of his own results. My opinion at the present time is distinctly in favor of a certain amount of antisepsis during all clean operations. We should attempt, up to the most minute detail, to render the surroundings of the wound aseptic; every assistant should wear gloves and a sleeved sterile gown; as little as possible of the skin about the incision should be exposed; the gloved hand should at inter-

¹ Centralblatt f. Chir., Band xxvii. p. 287.

² Beiträge zur klin. Chir., 1899, vol. xxiv. p. 129, and vol. xxv. pp. 371 and 457.

vals be immersed in 1 : 1000 bichloride ; should the glove or gown come in contact with anything not aseptic, it should be changed for a clean one.

The instruments and ligatures should be immersed in a carbolic acid solution. This prevents the slight danger of air infection in prolonged operations and re-disinfects during the operation the instrument which may now and then without notice come in contact with something not surgically clean. The sponges, instead of being dry, can be wet with 1 : 1000 bichloride. This amount of antiseptics seems sufficient in the great majority of clean cases. On the whole it is not necessary to irrigate the wound. Surgeons who are compelled to operate in bad surroundings, and with other circumstances which make asepsis very difficult, should in addition increase the antiseptic precautions.

Wound Drainage. On this subject there is also a great diversity of opinion. The drainage of a wound never lessens or prevents primary infection. If we know that a wound is distinctly infected it should never be completely closed. The extent to which it should be left open and drained depends upon the character and virulence of the infection and the condition of the tissues of the wound. The rubber drainage-tube introduced by Lister should seldom be used except now and then where there are large, deep, suppurating cavities, as in empyema and in abscess of the liver, in which, on account of the position of the abscess, the usual free incisions cannot be made. In clean wounds in which the opportunity for infection is only that just described in the previous section, there is only one indication for drainage, that is the prevention of a hæmatoma. Anschuetz,¹ on a basis of extensive clinical experience, comes to the conclusion that drainage is unnecessary in the majority of instances in clean wounds ; complete primary closure has many advantages ; the healing is more rapid ; there is distinctly less danger of secondary infection, and it diminishes the number of dressings.

The decision as to the drainage of the wound is a difficult one, but, on the whole, surgeons more and more are giving up drainage of clean wounds. The better one's technique and the more complete the hæmostasis the less necessity for drainage.

INFECTION.

Emphysematous Cellulitis ; Gas Bacillus Infection. THE IDENTIFICATION OF THE GAS BACILLUS WITH THE BUTYRIC-ACID BACILLUS. One of the most interesting observations since our last publication on

¹ Beiträge zur klin. Chir., Band xxv., Heft 3, p. 645.

gas phlegmon¹ is that of Schattenfroh and Grassberger, from the Vienna Institute of Hygiene². These two investigators have studied extensively the bacilli of butyric-acid fermentation, and find there are two groups: one non-motile producing spores, but with no flagelli, the other motile, also producing spores, but having flagelli; both are anaërobic, and are almost identical with each other in their various chemical and cultural properties. In the reading of the publications of E. Fränkel, on his bacillus phlegmon emphysema, and later investigations of the same bacillus by Hitschmann and Lindenthal, they were struck with its apparent identity with their non-motile variety of the butyric-acid bacillus. This resemblance had not occurred to Fränkel nor Hitschmann and Lindenthal, nor to Prof. Welch, who first isolated and described this bacillus, calling it the bacillus aërogenes capsulatus. The peculiar odor in milk cultures had been noted by Fränkel, and the butyric-acid and lactic-acid fermentation by Hitschmann and Lindenthal. We shall not go into details of the bacteriological study, but Schattenfroh and Grassberger are convinced that Fränkel's bacillus is identical with the non-motile form of the butyric-acid bacillus, which may become pathogenic both in man and animals. Their conclusions are based on the most careful bacteriological and chemical comparisons and animal inoculation. This places the "gas bacillus" in a well-known group of very widely distributed bacteria, but which we now know may become pathogenic under certain conditions in both man and animals.

So far they have been unable to demonstrate whether the motile variety of the butyric-acid bacillus is pathogenic.

Later Schattenfroh and Grassberger³ wrote that E. Fränkel, having sent them a pure culture of his bacillus, they were able to again confirm the identification. It is to be remembered (see *PROGRESSIVE MEDICINE* for 1899 and 1900) that the original investigators, Welch, Fränkel, and others, in their first studies of the gas bacillus did not demonstrate spores. These and later investigators have found that the gas bacillus is a spore producer under certain conditions.

THE RELATION OF THE NON-MOTILE BUTYRIC-ACID BACILLUS TO SYMPTOMATIC ANTHRAX (RAUSCHBRAND) BLACK-LEG. Schattenfroh and Grassberger, in the same article just quoted, make a preliminary report on the bacteriological study of the tissues from a few cases of symptomatic anthrax in cattle. They were surprised to find in three cases that they were able to isolate in pure cultures the non-motile butyric-acid bacillus, clearly identified by bacteriological, chemical, and animal inoculation tests, and they conclude that at least in these three

¹ *PROGRESSIVE MEDICINE*, December, 1900, p. 122.

² *Münchener med. Wochenschrift*, July 24 and 31, 1900, pp. 1032 and 1077.

³ *Ibid.*, December 11, 1900, p. 1733.

cases the bacillus must be the cause of the disease. In a few other cases which they studied they found a mixed infection; in every instance the non-motile butyric-acid bacillus and the bacillus which formerly has always been found in symptomatic anthrax were present, and sometimes other bacilli. Their investigations at present will not allow them to make positive conclusions. Symptomatic anthrax (Rauschbrand: This has been incorrectly translated "glanders" in the review of the *Philadelphia Medical Journal* for February 9, 1901, page 281) is an infectious disease not uncommon in cattle; the cellulitis is characterized by hemorrhages and marked oedema and a tendency to gangrene; to this characteristic the common names, "black-leg," "black spaul," and "bloody murrain," are due. I am unable to ascertain whether emphysema of the tissue is ever present. Schattenfroth and Grassberger do not speak of it. The non-motile butyric-acid bacillus which they isolated from the diseased tissue produced emphysematous phlegmon in guinea-pigs. Clinically we know that the gas bacillus of Welch and Fränkel has been cultivated from phlegmons in which there was no gas (I have observed three cases¹), yet the isolated bacillus produced gas phlegmon in guinea-pigs.

THE RELATION OF THE BACILLUS MUCOSUS CAPSULATUS TO GAS PHLEGMON. W. T. Howard² reports a case of general gaseous emphysema, with gas cysts in the brain, formed after death and due to the bacillus mucosus capsulatus. R. G. Perkins³ reports a laboratory epizootic among guinea-pigs, associated with gaseous emphysema of liver, spleen, and kidneys, from which he was able to isolate a bacillus identical with that of Howard, but Perkins thinks not identical with the bacillus aerogenes capsulatus of Welch. Howard thinks that perhaps the bacillus described by him may be the cause in some of the cases of gas phlegmon. The careful bacteriological work of Schattenfroth and Grassberger impresses one with the difficulty of the identification of these gas-producing bacilli found in emphysematous cellulitis.

THE CLINICAL SIDE OF EMPHYSEMATOUS CELLULITIS. From the cases reported in previous numbers of *PROGRESSIVE MEDICINE*, one quickly concluded that emphysematous gangrene can be recognized early clinically, and when so recognized early operative intervention, usually free incisions and, not of necessity, amputation, give most favorable results. B. F. Curtis reports a most interesting case.⁴ Here, in a man, aged fifty-two years, gangrene of the foot followed immediately after ligation of the femoral artery in Hunter's canal for popliteal

¹ *PROGRESSIVE MEDICINE*, 1899, 1900.

² *Journal of Experimental Medicine*, 1900, vol. v. No. 2, p. 139.

³ *Ibid.*, 1901, vol. v. No. 4, p. 389.

⁴ *Annals of Surgery*, October, 1900, vol. xxxii. p. 612.

aneurism. There was no evidence of infection in the gangrenous part and no emphysema. On the seventeenth day the leg was amputated in the upper third, and, as Dr. Curtis states, rather close to the gangrenous portion. There was no bacteriological or pathological report on the gangrenous leg. On the seventh day after the second amputation the stump looked red and œdematous; twenty-four hours later there was emphysema near the margin; no pain and no fever; the third amputation was immediately done in the medial third of the thigh. The wound healed by granulation, and there was no further emphysema. Dr. Curtis says that the *bacillus aërogenes capsulatus* was sought for, but not found. This case resembles closely the one that I reported;¹ here also gangrene followed ligation of the femoral artery in Hunter's canal for arterio-venous aneurism in the popliteal space. There was no emphysema in the gangrenous leg, but in the tissues and in the blood of the aneurismal sac we isolated pure cultures of the gas bacillus; there were also a very few gas bubbles in the blood in the aneurismal sac. I consider that it was quite probable that the gas bacillus reached the gangrenous part through the circulation, and in referring to the case Dr. Welch writes:² "With what we know of the entrance of intestinal bacteria into the circulation, there is nothing improbable in this opinion." Welch has collected from the literature two similar cases. These four observations demonstrate the possibility of the infection with the gas bacillus of an extremity already gangrenous from other causes, and this should be constantly borne in mind and should be an indication for immediate operation. Cover-slips made at the time of the operation would probably demonstrate the height of the infection. It was this observation that led me to the higher amputation in my case, with a most favorable result.

John B. Roberts³ reports the first case of emphysematous cellulitis observed in Philadelphia in which the *bacillus aërogenes capsulatus* was isolated. The bacteriological examination was made by Dr. Kneass. The injury was a compound fracture of the radius and ulna in a girl, aged twelve years; there was but a small wound of the skin made by one of the fragments of the ulna bone. Dr. Hardcastle made the first dressing and noted some earth near the open wound; the wound was carefully disinfected and dressed antiseptically; the patient was seen three hours later by Dr. Roberts; the arm was very much swollen and discolored, and there was crepitation; free incisions were at once made; twenty-four hours later an amputation was performed on the upper arm; the patient recovered. In dissecting the specimen Dr. Roberts found

¹ PROGRESSIVE MEDICINE, December, 1899, Case XXII., p. 173.

² Boston Medical and Surgical Journal, January 26, 1900, p. 7.

³ Annals of Surgery, June, 1901, vol. xxxiii. p. 768.

that the radial and ulnar arteries near the injury were thrombosed, but not lacerated; there was some gas in the tissues. I should infer that the gangrene in this case was due to thrombosis of the vessels associated with the injury; the rapidity of the gas bacillus infection is remarkable. Dr. Miller in the discussion stated that he found gas bubbles in the thrombus in the radial and ulnar arteries. Dr. Kneass reported that the cultures were pure. In this case the failure of a good result, after the early free incision, cannot be attributed so much to the gas bacillus infection as to the gangrene from the thrombus of the vessel.

EMPHYSEMATOUS CELLULITIS AFTER BULLET WOUNDS. Chas. E. Ferguson, of Indianapolis,¹ reports a case. The injury was a pistol bullet wound in the middle of the right leg. It was carefully dressed a few hours after the injury. Some hours later, because of complaint of pain in the wound, a careful examination was made. There was no evidence of infection. Temperature, 99.2°; pulse, 80. Inspection of the wound eighteen hours after the injury demonstrated an area of redness around the wound of entrance, and emphysema of the leg from the ankle to the knee. Temperature, 102.4°; pulse, 90. The cover-slip preparations from the discharge showed numerous large bacilli; at twenty-two hours the emphysema had extended above Poupart's ligament. Amputation was done at this time. The exact position is not noted. The patient recovered.

The interesting point in this case is that recovery took place, although the amputation was below the limits of emphysema. It is stated that the infection was pure, and the bacillus corresponds to that described by Welch in 1891. In my former report three of the twenty-one cases were bullet wounds; all recovered. There were two amputations and one incision.²

Recovery when the amputation was below the limits of emphysema has been recorded before. In Case XVII. of my first report,³ the emphysema of the shoulder, after amputation at the joint, disappeared, but the patient died, with symptoms of tetanus,⁴ on the fourth day.

Paul Thorndike, of Boston, reports two cases of recovery where the amputation was below the limits of the emphysematous cellulitis.⁵ The first patient (Case II., page 595) had a compound fracture of both bones of the right leg. The patient was very much shocked; six hours after

¹ Transactions of Indiana Medical Society, 1897, p. 339.

² The possibility of bullet wounds being infected with the gas bacillus is rare. Among about sixty cases in the Johns Hopkins clinic during twelve years, we have observed but two cases. It is much more common after compound fractures.

³ PROGRESSIVE MEDICINE, December, 1899, p. 171.

⁴ Mixed infections of the gas bacillus and tetanus have been reported previously by E. Fränkel (Münchener med. Wochenschrift, 1899, Nos. 42 and 43).

⁵ Boston Medical and Surgical Journal, June 7, 1900, vol. cxlii. p. 592.

the accident, under ether narcosis, the wound was thoroughly disinfected, and the fragments approximated; on the third day evidence of gangrene of the foot and toes was present; on the fourth day emphysema as far as the middle of the thigh was noted; amputation was performed at the middle of the thigh through the emphysematous tissues, and the wound left open; the emphysema extended, and in three days reached Poupart's ligament. At this time, under ether, the emphysematous tissue was freely incised. The patient made an uninterrupted recovery. The infection in this case was mixed, streptococci, staphylococci, and the gas bacillus. Unfortunately cultures were only taken from the gangrenous tissues, and not from the emphysematous cellulitis above the point of amputation. The early gangrene of the foot in this case indicates that there had been a rupture of thrombus of one or both tibial arteries.

The second case (Case III., page 596) was a compound fracture of both bones of the forearm in a boy aged twelve years. Shortly after the injury the wound was thoroughly disinfected and placed in plaster-of-Paris. Delirium and fever were present shortly after the operation; in twenty-four hours swelling and discoloration of the arm; in forty-eight hours emphysema of the entire arm, extending over the chest. Amputation was performed just below the shoulder-joint through the diseased tissues, the wound being left open. The patient recovered. The pathological report showed no emboli or thrombosis in the vessels of the arm. There was no bacteriological report, as this case was observed previous to Welch's publication on gas bacillus.

Mr. George Heaton¹ also reports a case of compound fracture of the radius and ulna followed by emphysematous cellulitis of the entire arm. An amputation of the shoulder-joint was performed on the fourth day after the injury. It is noted that gas bubbles came from the cut surfaces, and the flaps were emphysematous; the wound was left open; the emphysema disappeared from the flap in twenty-four hours; the patient recovered.

These recoveries demonstrate the truth of the conclusions in my first publications, that emphysematous cellulitis is frequently relieved by free incisions when performed early and when the destruction of the soft parts has not been extensive. Muscatello and Gangitano,² as quoted by Welch,³ take similar positions as to prognosis and treatment.

English surgeons do not seem to be familiar with the correct bacteriology of emphysematous gangrene, nor with the better prognosis, even after conservative treatment. Mr. J. Jackson Clark⁴ writes as

¹ *Lancet*, 1899, vol. i. p. 898.

² *Riforma Medica*, 1900, ii. pp. 508, 519, and 530.

³ *Loc. cit.*

⁴ *Lancet*, 1899, vol. ii. p. 1229.

follows : "The rapid spread of emphysematous gangrene is very striking, and is the chief cause of the unfavorable results which in most cases follow amputation for this disease, for unless the limb is removed early the œdema will have extended so far that the incisions have to pass through affected tissues, though even under such circumstances occasional recoveries have been recorded. The proportion of recoveries after amputation for this condition is a low one, one in twenty-five cases." Mr. Clark also incorrectly states that the bacillus of malignant œdema is usually the cause of the emphysematous gangrene.¹ Mr. Heaton² also writes : "It is now generally admitted that the majority of cases of spreading traumatic gangrene are due to the presence of the bacillus of malignant œdema." I am unable to find any reports by English surgeons familiar with the work of Welch and Fränkel on the bacteriology of emphysematous gangrene.

EMPHYSEMATOUS CELLULITIS IN INCISED AND LACERATED WOUNDS. I have previously reported two cases (Cases XV. and XVI.),³ one over the scapula and one of the scrotum. In these cases, although the gas bacillus was present, there was no emphysema. Both recovered after the wounds were laid wide open. Welch mentions a number of other instances in which the gas bacillus was present in the tissues without emphysema. Pratt and Fulton, of the Boston City Hospital,⁴ have recently recorded a similar observation. The condition was carcinoma of the bile duct ; death followed operation ; the autopsy showed multiple abscesses of the liver from which the gas bacillus was isolated. There was no gas. L. M. Loeb, of Chicago, has recently recorded⁵ a lacerated wound infected with the gas bacillus in which there was extensive emphysema. The patient recovered without amputation.

EMPHYSEMATOUS PHLEGMON. In *PROGRESSIVE MEDICINE* for December, 1899, page 171, I recorded four cases where the emphysematous gangrene could be considered non-traumatic. If an injury were present it was very slight. Loeb (*loc. cit.*), of Chicago, has recently recorded a case of this character. The patient, a male, aged forty-three years, was taken suddenly with pain in the left shoulder ; after two days an area of infection appeared over the deltoid ; examined on the fifth day, there was an ulcer over the shoulder, surrounded by an area of emphysema ; free incisions were made through the ulcer (the area of infection was not excised) ; the infection and emphysema increased, and the patient died. Autopsy : emphysema and œdema of the entire body ; chronic tuberculosis and œdema of the lungs ; gas in heart's blood and

¹ *PROGRESSIVE MEDICINE*, December, 1900, pp. 122-123.

² *Loc. cit.*

³ *Boston Medical and Surgical Journal*, June 17, 1900.

⁴ *American Medicine*, July 27, 1901, vol. ii. No. 4, p. 137.

⁵ *Loc. cit.*

bile. The cultures demonstrated a mixed infection; the bacillus *aërogenes capsulatus*, staphylococci, streptococci, and colon bacilli.

EMPHYSEMATOUS CELLULITIS AFTER COMPOUND FRACTURES. This is most common. Welch¹ records eighteen out of forty-six cases. In the eight cases which I have previously reported² there were 50 per cent. of recoveries. Delay in treatment can certainly explain some of the deaths. The recent cases just discussed decrease the mortality. In estimating the proper treatment of a compound fracture infected by the gas bacillus or any other bacteria, we must bear in mind the extent of the destruction of the soft parts and the possibility of gangrene due to injury of the bloodvessels. Such injuries themselves are an indication for an amputation. If there is no infection we may delay. With the first appearance of any infection operation should be performed at once. Amputation is indicated if there is any appearance of gangrene of the extremity, but experience has demonstrated that it is not always necessary to amputate above the point of emphysema. The gangrenous part should be removed, but the infection of the limb above the point of gangrene has frequently been relieved by an open wound and free incisions.

Conclusions. More recent experience has confirmed our earlier estimate of the more favorable prognosis in emphysematous cellulitis, and that amputation is not always necessary if the disease is recognized in the early hours and when the operative treatment is based upon not only the infection but the extent and character of the destruction of the soft parts from the original injury, especially the possibility of injury to the artery.

More careful and more complete bacteriological studies of recent wounds, both infected and non-infected, and a more careful description of the exact character of the original injury will, without doubt, aid us in placing the treatment of emphysematous cellulitis and other infections on a more scientific basis. The occurrence of emphysematous cellulitis associated with diabetes or glycosuria needs more accurate observation.

Malignant Œdema. This has been previously fully discussed,³ and Professor Welch was then quoted in the following statement: "The whole subject of human malignant œdema is one which needs thorough revision and investigation by more exact bacteriological methods than have yet been applied to it." Welch was able to find in recent reports only one case (Brabec's) in which the identification of the malignant œdema bacillus seemed satisfactory. In this case the œdema was

¹ Loc. cit.

² PROGRESSIVE MEDICINE, December, 1899, pp. 164, 167.

³ Ibid., December, 1900, p. 122.

hemorrhagic, but there was no gas. In the literature of the last year I have been able to find only one case, and, unfortunately, I have been unable to get the original article (Eisenberg¹). In the review it is stated that malignant œdema of the upper extremity followed an injury to the hand. From the tissues the bacillus of malignant œdema was isolated and the diagnosis confirmed by animal experiments. Pyogenic cocci and the colon bacilli were also present. No mention is made of gas in the review.

In the majority of text-books on surgery and surgical pathology the clinical picture of malignant œdema does not differ from that of emphysematous cellulitis in which Welch, Fränkel, and others have found the bacillus *aërogenes capsulatus*. Both lead to gangrenous processes characterized by a hemorrhagic exudate and the development of gas.

Infections in human beings in which the chief characteristic is a hemorrhagic exudate, and which may be associated with a septicæmia, the metastatic lesions of which are also hemorrhagic, is well known. In these cases a number of different bacteria have been described as the infecting agents. The entire subject, with full literature, has recently been discussed by W. T. Howard, Jr.,² and George Blumer and Arthur T. Laird.³ These investigators demonstrated an anaërobic bacillus belonging to the group bacillus *mucosus capsulatus*.

There is much room for future comparative bacteriological study of the bacillus of malignant œdema, the bacillus *aërogenes capsulatus*, the bacillus *mucosus capsulatus*, with the bacilli of butyric acid fermentation discussed in the first part of this section.

DIABETIC GANGRENE.

This name, diabetic gangrene, is now considered by most authorities to be a misnomer. Cuthbert S. Wallace⁴ reports on twenty-six cases observed during eleven years at the St. Thomas Hospital in London. In twenty-four of these cases in which there was an opportunity for examining the arteries, well-marked atheroma was present in every instance except one. During the last five years Wallace has made microscopical examination of the arteries, and in every case demonstrated sufficient arterial changes to explain the gangrene. For this reason he concludes that the disease is of arterial origin, and should be considered as arterial gangrene complicated by glycosuria.

¹ *Przegląd Lekarski*, 1899, Nos. 45, 46; reviewed in *Centralblatt f. Chir.*, 1900, Band xxvi. No. 6, p. 173.

² *Journal of Experimental Medicine*, March, 1899, vol. iv. p. 149.

³ *Johns Hopkins Hospital Bulletin*, February, 1901, vol. xii. p. 45.

⁴ *Lancet*, December 23, 1899, vol. ii. p. 1730.

Wallace's Conclusions. 1. That it yet remains to be proved that true gangrene (excluding death from acute specific processes, which may occur in any subjects and at any age) occurs in diabetic patients unaccompanied by such arterial disease as would of itself produce gangrene.

2. The glycosuria may or may not precede the gangrene, but is not usually accompanied by other signs of diabetes.

3. That septic wounds may produce a glycosuria which vanishes when the septic process is removed.

4. That individuals suffering from septic processes are often on the borderland of glycosuria.

5. That gangrene may aggravate a pre-existing glycosuria.

6. That the arterial disease is sometimes that which accompanied or is produced by chronic renal disease.

7. That it has yet to be proved that neuritis can produce any gangrene comparable to that of the so-called diabetic gangrene.

8. That the best chance of recovery is offered by removal of the limb near the trunk, and that this measure should be undertaken before the patient is reduced by septic absorption.

9. That the presence of glycosuria may be an indication, instead of a contraindication, for operation.

Collective Review on Diabetic Gangrene and its Treatment.

The most interesting and instructive publication on diabetic gangrene and its treatment is a recent résumé by Heinrich Wolf,¹ of Vienna, with 172 references to the literature, beginning with 1880. The first part of the work is a discussion of the cause of gangrene and the various inflammatory conditions which clinically, we know, are very common complications of diabetes. The clinical observations and the great number of experimental investigations have given rise to various views from which we may make the following conclusions: The disease diabetes is not the cause of gangrene *per se*, but the diabetic patient always has changes in the vessels due to arterio-sclerosis which explain the gangrene. The cause of gangrene in the diabetic is, therefore, the same as in any other individual not diabetic. On the whole the prognosis of gangrene in the diabetic is somewhat worse (the arterial changes being equal) than in the non-diabetic patient. Diabetes is not the cause of the various inflammations which are so frequently observed during the course of this disease, for example, carbuncle; but the resistance of the diabetic patient to the various infections seems to be very much less than the ordinary non-diabetic individual, and for this reason infections which in the healthy would be easily taken care of by the affected tissues assume a very grave character in the diabetic. The tendency to

¹ Centralbl. für die Grenzgebiete der Medicin und Chirurgie, 1901, Band iv., Heft 1.

spread locally, to become gangrenous, and to general infection is increased. The knowledge that a patient is suffering from diabetes should increase the vigilance of our surgical treatment. Local infections or gangrene in diabetes demand an earlier and more radical operative interference. The area of infection should be more widely excised because we can depend so little on the tissues to aid in the localization and the resistance to the infection. In the treatment of gangrene due to arterio-sclerosis we are also influenced not only by the presence of diabetes but by the condition of the arteries in the affected limb.

Patients suffering with diabetes (and it is unnecessary to state that they should be under the proper diabetic treatment) should be informed of the added dangers of small wounds and infections, and should be instructed to seek medical attention at once. A small furuncle, especially at the back of the neck, a slight infected wound of the finger, a small wound made by paring a corn, all—if neglected—in the diabetic patient may rapidly extend into a very serious inflammation. It should also be remembered that the presence of sugar in the urine alone is not a positive indication of diabetes, and this glycosuria may frequently be the result of the infection. Without much doubt many cases of so-called diabetic phlegmons were simply cases of phlegmon in which the glycosuria was secondary. The prognosis in such cases is always better than when diabetes is present.

The resistance of the diabetic patient to infections, the danger of operative interference, and the dangers of narcosis, however, seem to be frequently exaggerated by the general profession. An individual suffering from diabetes, with the disease under proper control, does not seem to be a specially bad subject for narcosis. The healing of the wound is generally just as good as in any other individual, if proper precautions are taken.

Diabetes, therefore, cannot be considered a positive contraindication to any necessary operative interference. We, however, need further observations on this point.

All authorities agree that the surgical complications of diabetes should be divided into two groups: 1. Phlegmons, the cause of which in every case is a distinct infection, and in which, on account of the lower resistance of the tissues, behaves somewhat differently than similar infections in the healthy individual. The infection tends to spread rapidly, the onset of necrosis and gangrene is early, rapid, and extensive. These features are increased if the circulation is impaired by arterio-sclerosis, or the presence of lesions in the peripheral or central nervous system, which are not uncommon in diabetes, for example, multiple neuritis or lesions in the posterior column of the cord similar to

those in pernicious anæmia.¹ 2. Gangrene, of which two types must be distinguished: (a) the inflammatory, (b) the non-inflammatory. In both the primary cause of the gangrene is arterio-sclerosis. In gangrene from arterio-sclerosis in non-diabetic patients we also have the inflammatory and the non-inflammatory types; but it seems that in diabetes the inflammatory type is much more common. The inflammation is due to the infection of the tissues in the region of the gangrenous part due to the lowered resistance from faulty circulation and to the easy portal of entrance through the gangrenous part. The treatment of phlegmons and the inflammatory type of gangrene in diabetes should be much more energetic and as early as possible, while in the non-inflammatory type of gangrene we may wait for the line of demarcation and confine our excision to the gangrenous parts only.

Considering the causes of phlegmons and gangrene in diabetes, Wolf makes the following very natural division: 1. The impaired vitality of the cells in diabetes. 2. The presence and virulence of the micro-organisms. 3. Lesions of the vessels. 4. Lesions of the nerves. 5. Alcoholism.

THE IMPAIRED VITALITY OF THE CELLS IN DIABETES. We know that in diabetes mellitus an excessive amount of sugar accumulates in the blood, the index of which is the amount found in the urine. The sugar found in the urine is glucose, and before we can consider the disease true diabetes the glycosuria must be continuous and present for a number of months. Much has been written on the cellular changes in diabetes, with the result that we know that there is great impaired vitality. Whether this is due to the direct action of the sugar or to other causes we are still uncertain. Next to the presence of sugar in diabetes, lesions of the pancreas and the kidney are most constant. Lesions of the pancreas are present in 50 per cent. of the cases (Hansmann, quoted by Osler). Chronic diffuse nephritis is very common. Therefore, surgeons when contemplating narcosis and operative interference in diabetic patients must bear in mind the general impaired nutrition and the lowered resistance of the cells, and the possible presence of nephritis.

MICRO-ORGANISMS. On the whole, clinical observation and experimental investigations have demonstrated that "it is not the microbe which is especially virulent, but it is the organism which is debilitated." There is no reason to believe that the presence of sugar in the blood or tissue increases the virulence of the present micro-organisms or creates a more favorable culture medium; in fact, certain micro-organisms, streptococci and staphylococci, grow badly on media containing 5 per cent.

¹ Williamson, quoted by Osler, *Text-book on Medicine*, third edition, 1900.

of sugar (Bujwid and Grossmann). The increased tendency to necrosis and gangrene in diabetic phlegmons cannot be explained by increased virulence or a specific micro-organism.

LESIONS OF VESSELS. O. Israel¹ in 1882 was the first to point out the frequent coincidence of arterio-sclerosis and diabetic gangrene, and since this time the observations of all other authorities have confirmed those of Israel. On the frequency of gangrene Wolf makes the following table :

Age.	Table showing frequency of diabetes mellitus.			Table showing frequency of gangrenous affections.					
	Pavy, 1860 cases	Frerichs, 400 cases	Griesinger, 225 cases	Wolf's statistics.					
				Girou, 128 cases	Mayer, 39 cases	Grossmann, 177 cases	Inflammatory, 54 cases	Non-inflammatory, 64 cases	Total, 118 cases
	Per ct.	Per ct.	Per ct.	Per ct.	Per ct.	Per ct.	Per ct.	Per ct.	Per ct.
Under 10 years	0.58	1.25	19.35
10 to 20 "	4.19	7.15	
20 " 30 "	7.13	10.50	25.80	2.44	3.88
30 " 40 "	16.47	17.75	27.65	8.94	5.0	10.16	4= 7.41	2= 3.3	6= 5.1
40 " 50 "	24.92	25.25	16.95	17.08	25.0	20.83	12=22.2	11=17.2	23=19.5
50 " 60 "	30.73	26.25	6.45	36.50	30.0	40.67	28=51.8	22=34.4	50=43.3
60 " 70 "	13.37	10.50	3.23	21.13	23.0	19.20	4= 7.41	18=28.1	22=18.6
70 " 80 "	2.49	1.25	0.92	13.32	17.0	6.21	3= 5.59	4= 6.15	7= 5.93
80 and over	0.07
Unknown	3= 5.59	7=10.85	10= 7.57

We see at once from this table that gangrene in diabetic patients is most commonly found in the ages in which we know arterio-sclerosis and its results are most prevalent. Seventy-nine out of 118 patients, or 66.9 per cent., were over fifty years of age. Wolf and Mayer record no cases of gangrene in diabetes under thirty years of age. Girou and Grossmann report a few cases between twenty and thirty years. These cases, and most of those up to forty years of age, are probably explained by the presence of arterio-sclerosis in young individuals (presenile gangrene). I have been unable to find any statistics to demonstrate that presenile gangrene is more common in diabetic patients. From Wolf's own statistics, attention to which he calls, the inflammatory type of gangrene is more common in the earlier decades. Wolf notes that the relative infrequency in the female, the rarity of the gangrene in the upper extremity, and the frequent history of alcoholism, and the usual advanced age of the patient, all emphasize the importance of considering arterio-sclerosis the chief factor in the cause of diabetic gangrene.

¹ Berliner klin. Wochenschrift, 1882, p. 275.

The anatomical findings in the vessels correspond exactly to those of gangrene not associated with diabetes, to be discussed later.

LESIONS OF THE NERVES. It is a question whether the affection of the nerves is primary or secondary to the arterial changes. Wolf considers this question unsolved. Without much doubt, lesions of the peripheral nerves, whether primary or secondary to arterio-sclerosis, increase the dangers of phlegmon and gangrene in diabetes.

ALCOHOLISM. The consensus of opinion with regard to alcohol is that it should be considered only an indirect cause of the inflammatory and gangrenous complications of diabetes.

Wolf concludes that diabetes alone cannot produce gangrene, and that it is erroneous to use the term diabetic gangrene.

Glycosuria as a Consequence of Gangrene. Many authorities, Redard,¹ Rosenbach, König, and others, claim that in many cases of gangrene, glycosuria appears (*diabète éphémère*). I have recently observed such a case. Schiff (quoted by Vergily)² produced experimentally, by ligating the veins of the extremity, gangrene with temporary glycosuria. Grossmann opposes this view, but Wolf is of the opinion that there are sufficient clinical observations to demonstrate that temporary glycosuria may be associated with some cases of gangrene, especially of the inflammatory type, and more frequently with grave phlegmons, and this glycosuria cannot be considered diabetic.

The Treatment of Phlegmons in Diabetes. Wolf considers this part of the subject only superficially, but as stated in the introduction, the surgical principles are pretty well established. In the diabetic patient the treatment of any infection, no matter how slight, becomes a much more serious affair than in the non-diabetic individual. We should never limit our operative interference to small incisions, but the area of infection, if possible, should be completely excised. Spreading phlegmons on the extremities may demand early amputation. Treated early and in this energetic way the phlegmons in diabetes usually are easily cured. Delay in the treatment or partial operative interference are followed by disastrous results. My own experience with the complete excision of carbuncle in diabetic patients, and some radical measures in other phlegmons, has been most satisfactory.

The Treatment of Gangrene in Diabetes. We are influenced here in our choice of operative and non-operative measures by a number of factors: the general condition of the patient, the character and extent of the gangrene, the presence of or absence of cellulitis, lymphangitis, or phlebitis above the gangrene, and the condition of the large vessels

¹ *Revue de Chirurgie*, 1896, p. 639.

² *Gaz. Hebd. de Méd.*, 1893, vol. xi. No. 32, p. 376.

in the extremity the seat of the gangrene. It must be remembered that the general condition of the diabetic patient is temporarily made very much worse by the presence of the infection, and experience has demonstrated that after the radical treatment of the infection we are pleasantly surprised by a very rapid improvement in the general condition, and even a diminution of the percentage of sugar in the urine. For this reason we should not allow even a very critical general condition of the patient to influence us against operative intervention. The prognosis may be bad enough, but it is distinctly worse if conservative measures are adopted. In fact, a bad general condition associated with a not very grave local condition is a more urgent indication for an early and radical operative interference than the reverse. An infection (cellulitis, lymphangitis, or phlebitis) above the area of gangrene is an indication for immediate operative intervention irrespective of the general condition, and we must not only remove the area of gangrene, but the area of infection as well. As a rule, irrespective of the condition of the vessels, higher amputation should be done in the inflammatory type of gangrene than in the non-inflammatory type. The presence of ascending infection increases the probability of more extensive thrombosis of the larger vessels of the limb which may not have been present before the onset of the infection.

In a few cases of non-inflammatory gangrene confined to the toes we can wait for the line of demarcation, especially when the general condition of the patient is good, and then remove the gangrenous toe only under local anæsthesia. When the gangrene extends to the foot operative interference should not be delayed an instant. Experience has demonstrated that amputations of the foot or ankle are unsatisfactory. Gangrene of the stump usually follows, and the higher amputation becomes necessary. In deciding upon the higher amputation, leg, knee, lower or upper thigh, we are influenced by the general condition of the patient and the conditions of the arteries in the limb. If the patient's general condition is not good, and especially when pulsation is absent in the tibial or popliteal arteries the amputation should be done at once in the thigh; if the femoral pulsation is absent, in the upper thigh. When the general condition of the patient allows a longer narcosis, and pulsation is made out in the tibial vessels, we may amputate somewhere in the middle third of the leg. If during the dissection (which should always be done without an Esmarch) we find that the circulation of the tissues is very poor, we should amputate at the knee or at the lower thigh. Complete thrombosis or obliteration of the popliteal artery is an indication for a thigh amputation, although some surgeons have had good results with the Gritti amputation at the knee. The individual experience of surgeons in diabetic gangrene is usually limited, and with

hardly an exception every surgeon has in a certain number of instances found it necessary to amputate higher, due to gangrene of the stump of the first and lower amputation. This clearly demonstrates that as yet we cannot formulate positive rules as to the exact selection of the seat of the first amputation. Fortunately the records show that there has been little if any increase in the mortality in these double or even triple amputations. The cases seem to fall naturally into three groups : 1. Those in which the gravity of the local condition or the extent of the arterial changes demand at once the highest amputation. There is no question in the mind of the surgeon as to the point of selection. In this group of cases the general condition of the patient is generally bad and the mortality high. 2. Those patients whose general condition is excellent, the gangrene of the non-inflammatory type and confined to one or more of the toes. Here, as a rule, we can use conservative measures, and even if later we find it necessary to amputate higher the delay does not increase the mortality, while by such conservative treatment we save many patients from the mutilation of higher amputations. 3. Here we feel that an amputation is indicated, but it is difficult to tell from the local condition the better position. There are too many good results in the literature and in one's own experience to allow the surgeon to perform a high thigh amputation in every instance. If the patient's general condition is good he should be given the benefit of the doubt, and a lower amputation performed. The stump should be frequently examined, and the first appearance of gangrene in the flap or signs of infection should be followed at once by an amputation at the highest point. On the whole, the surgeon will be influenced more by the careful observation of all the facts in the individual case than by the establishment of any general rule. On the whole, amputation for gangrene in diabetes in the last few years has given most satisfactory results.

The Dangers of Operation in Diabetes. Wolf's review of this part of the subject shows the great difficulty in estimating the dangers and the factors of the mortality. Any patient suffering from diabetes may suddenly develop diabetic coma, which is usually fatal. Infections increase this danger, and it may be said with truth that many of the deaths after operations for phlegmons and gangrene in diabetes occur in spite of the operation, and are not due to the operation, which, without doubt, promised the only hope of relief.

The increased dangers of narcosis in diabetes are not thoroughly established. Many authorities claim that narcosis increases the danger of diabetic coma, others that the narcosis has no influence in producing the coma. Wolf gives the following figures : Of 110 patients suffering from diabetes and gangrene 50 died ; of these 19, or 17.2 per cent.,

in coma ; 22 of the 50 deaths were not subjected to operative interference ; of these 6 (27.3 per cent.) died in coma ; 28 of the 50 deaths followed operation ; 13 (46.4 per cent.) died in coma. These figures indicate the increased danger of narcosis. The question, however, can be naturally asked, but not answered, what would have been the mortality of these 28 deaths after the operation if no operation had been performed ? It seems pretty clear that if an operation is indicated its dangers are less than delay or conservative treatment. We probably can lessen the danger of general narcosis by shortening the interval and diminishing the amount of the narcotic, or substituting local anæsthesia. Our experience, however, with local anæsthesia in operations for phlegmons and gangrene in diabetes is not yet sufficient to judge of the result. Wolf is of the opinion that infiltration anæsthesia by Schleich's method near the area of gangrene or infection increases the danger of the extension of the gangrene or the infection. This is probably true ; but when the operation is an amputation and at a point at some distance from the area of gangrene or infection, the probabilities are that it could be done satisfactorily with the other methods of local anæsthesia. The usual dangers and post-operative complications of the general narcosis are probably greater in diabetic individuals, especially lung complications and the effect of the anæsthetic on the kidneys, because we know that pneumonia in diabetes is a very serious infection, and chronic nephritis is usually present.

The Mortality of Non-operated and Operated Cases of Gangrene in Diabetes. According to Wolf's figures, 110 patients, there were 50 deaths, making a general mortality of about 45 per cent. Thirty-five cases were not operated upon, and of these 22 died, a mortality of 63 per cent. Of these 22 cases of death 6 died from coma, 13 from infection from the area of gangrene and 3 from other causes stated as collapse, emboli, asthma (?). Among 75 cases subjected to amputation there were 28 deaths, a mortality of 37 per cent. ; of these 17 died of sepsis and 11 from coma. These figures are greatly in favor of the operative treatment. One of the cases operated on was in collapse, but recovered. The 17 cases which died in coma, 6 non-operative and 11 operative, had probably reached such a grave stage of the disease (diabetes) that little could be done to influence the result. It is even a question whether those who developed coma after operation would not have succumbed if not subjected to operation. In the non-operative cases which died of sepsis, it is a question whether, if they had come to treatment earlier, an operation would not have given a better result. The figures also show that second amputations have not increased the mortality. Of 63 primary operations there were 25 deaths, or a mortality of about 40 per cent., while in the 12 patients

subjected to secondary operations there were 3 deaths, a mortality of 25 per cent. The 1 subjected to a triple amputation recovered. Those patients subjected to second operations had unquestionably better local and general conditions, and these figures demonstrate that one can be conservative in selected cases without increasing the mortality.

The study of the results of amputations at different levels is also instructive, especially with regard to the treatment of inflammatory and non-inflammatory gangrene. The contrast is especially marked in amputation of the toes for inflammatory gangrene. Here we have 9 cases of primary amputation of the toes. Only 3 healed and recovered, in 6 it was necessary to do a second amputation. Of these 3, or 50 per cent., died of sepsis, in 2 the amputation was at the knee, in 1 at the thigh. Three recovered, in 2 amputation at the thigh, in 1, first a Charcot, then a thigh amputation. In 8 cases of non-inflammatory gangrene confined to the toes, in 5 there was healing and recovery after the primary amputation of the toe. In the remaining 3 cases it was necessary to do a second and higher amputation; all recovered. These figures demonstrate that amputation of the toes for inflammatory gangrene in diabetes is seldom justifiable, while in the non-inflammatory form it is the operation of choice unless the examination of the pulse in the vessels of the limb demonstrates thrombosis and obliteration of the larger trunks.

Amputation at the ankle-joint, Pirogoff or Syme, does not seem to be a good procedure in either form of gangrene. Of 5 cases, only 2 healed and recovered. One died of sepsis (inflammatory) and in 2 it was necessary to do a thigh amputation (both recovered with non-inflammatory gangrene).

These figures demonstrate that amputations below the knee give, on the whole, better results than amputation at the knee (Gritti or ex-articulation). Of 8 amputations at the knee, 4 healed and recovered, 4 died, 50 per cent. (3 of sepsis, 1 of coma), while among 20 amputations at the leg recovery took place in 14 instances, deaths in 5, only 25 per cent. In one case (inflammatory gangrene) it was necessary to do a secondary thigh amputation; the patient however recovered. The better results in lower leg amputations over amputations at the knee are equally true for the inflammatory as for the non-inflammatory gangrene.

The mortality of primary thigh amputations is about the same in both types of gangrene, 50 per cent., but as nine of the sixteen deaths were due to coma the probabilities are that these patients were in very bad general condition. Of the eight cases of secondary thigh amputations (patients in good general condition) only one died.

The good results of amputations through the leg (*Unterschenkel*)

demonstrate that it is by no means always necessary to amputate above the knee, and also that amputations at the ankle and knee-joints are not good surgical procedures for diabetic gangrene. From these figures we might establish this general rule: When the amputation cannot be confined to the removal of the toe or toes the point of selection should be the leg at a sufficient distance beneath the knee to make a useful stump. If the condition of the circulation or the vessels of the leg is not good the amputation should be performed at the thigh, usually the lower third.

The mortality in Wolf's statistics is without doubt increased because the cases have been collected from both older and recent literature. Recent reports of individual surgeons with a smaller number of cases, about eight to ten, show a greatly decreased mortality, a few with no deaths (Lindner six cases, Bunge four cases).

The experience in Prof. Halsted's clinic at the Johns Hopkins Hospital has also been more favorable. The number of cases, however, is small. Among thirty-five cases of gangrene, eight have been associated with diabetes. All these eight cases were over fifty-five years of age, and clinically were all associated with arterio-sclerosis. There were two deaths; one patient not operated upon was admitted to the hospital in a condition of coma, and died in a few hours; the second patient suffered with inflammatory gangrene involving the heel. The first operation consisted of an excision of the gangrenous area, but it was necessary later to do an amputation of the leg at the junction of the middle and lower third. Four days later it was necessary to open the stump for infection, and the patient died in coma on the ninth day after operation. This patient was under my own observation, and I believe now that it would have been better surgery, in view of the character of the gangrene and the beginning infection above it, to have amputated in the thigh at first. In four cases, typical pictures of senile gangrene, we amputated the toes only, two under cocaine. In two cases the primary amputation was at the leg; in both of these cases the gangrene extended to the foot; in one case in which the gangrene was confined to the toes and foot it was necessary, after an amputation at the lower leg, to perform a second amputation through the lower third of the thigh. All these patients recovered. One case is of especial interest. A male, aged sixty-three years, suffering with diabetes for three years, was admitted to the hospital with gangrene of the second toe of three months' duration. The general condition was excellent, and he had been under rigid dietetic treatment for three years. I removed the toe at the phalango-metatarsal joint; the wound healed per primam. In six months he returned with gangrene of the little toe of the same foot; this was also amputated, with a good result. A year later the

third toe was removed, and about one year later, because of gangrene of the remaining toes, an amputation was performed by Dr. Cushing at the tarsometatarsal joint. The patient is living and the foot is a very useful one. This patient has general arterio-sclerosis, but the pulsation is present in both tibial arteries. The pathological examination of the vessels in the removed specimens demonstrated endarteritis and thrombosis.

I recently had an observation on gangrene confined to the toe which has been very instructive. The patient was a male, about fifty-five years of age, who, during the six months previous to the onset of his trouble had noticed an impairment of his general health ; his appetite was not as good, he easily tired, and got short of breath on exertion. Ten days before I first saw him he noticed two boils on the back of the neck, which were incised under cocaine anæsthesia. The inflammation, however, of the cellular tissue on the back of the neck increased in spite of numerous small incisions. At my first examination there was a large carbuncle occupying the centre of an area of diffuse infiltration which extended over almost the entire posterior part of the neck. The patient's temperature was 102° , pulse about 120 (this fever and rapid pulse had only been present about twenty-four hours). The urine contained much albumin, numerous hyaline and granular casts and sugar. The blood showed slight anæmia and a leucocytosis of about 15,000. The entire area of infection was completely excised under partial and interrupted chloroform narcosis. After two or three days the sugar disappeared from the urine, and the albumin and casts decreased. The convalescence was uninterrupted, the general condition improved, and the wound after the separation of some gangrenous parts of muscle and tendon rapidly filled with healthy granulation tissue. After about three weeks, when the patient had been walking about for two or three days, he noticed pain at the base of the third toe of the right foot ; in twenty-four hours he noticed discoloration. The patient was then readmitted to the hospital and put to bed. The urine again showed a trace of sugar, but the albumin and casts had not increased. The palpable peripheral arteries showed slight evidences of sclerosis ; the pulse of both tibial arteries in the affected limb was, however, good. The area of gangrene did not extend. After waiting a few days three toes were amputated, removing the heads of the adjacent metatarsal bones. This was done because it would have been impossible to remove the gangrenous toe completely without interfering with the circulation of the adjacent toes. At the operation the tendons were divided as high as possible. The circulation of the divided tissues appeared excellent. The digital arteries bled. The wound was not closed, but allowed to fill with blood clot. The sugar disappeared from the urine, and at the

end of the month also the albumin and casts. The most interesting observation was the sloughing and separation of every tendon divided at the operation, which delayed the ultimate healing of the wound for a number of months. The patient has now a very useful foot.

Spontaneous Gangrene in Youthful Individuals; Presenile Gangrene. On this subject Prof. Welch writes:¹ "Of special interest is the relation of thrombosis to certain forms of so-called 'spontaneous gangrene' which may occur in middle life, or even in the young, and are often preceded by definite symptoms indicative of gradual occlusion of the arteries. Von Winiwarter concluded from his examinations of several cases that the primary disease is an obliterating endarteritis resulting in complete closure of the affected vessels. Zoege von Mantuffel, however, finds that thrombosis participates, in an interesting way, in the gradual occlusion of the arteries. According to him, by the deposition and organization of successive layers of parietal thrombi, the arteries which are usually the seat of a primary sclerosis gradually become filled with vascularized connective tissue. Haga considers this endarteritis thrombotica to be syphilitic. Hoegerstedt and Nemser believe that in general the deposition and organization of parietal thrombi are common and important processes in angiosclerosis. Von Recklinghausen has described hyaline thrombosis of small arteries in spontaneous and arteriospastic gangrene."

On this subject I find three very interesting recent publications by Bunge,² Matanowitsch,³ and Wulff.⁴ In these three articles we get a complete résumé of the rather brief literature. Bunge and Wulff confine themselves chiefly to pathological studies, and Matanowitsch is entirely a clinical study. Bunge's publication is the most exhaustive; he describes and illustrates the pathological picture in fifteen cases, five each of senile, diabetic, and presenile gangrene—thirty-one figures illustrating the histological picture of the arterial changes and three colored plates containing twelve figures. Bunge establishes without doubt the uniform arterial changes in these three forms of gangrene, confirming what has been previously written in the section on diabetic gangrene.

Résumé of the Literature on Spontaneous Gangrene. Friedländer,⁵ in 1876, seems to have been the first to describe the condition and used the term endarteritis obliterans. His observations were confined to the smaller vessels. Later Winiwarter⁶ found this pathological con-

¹ Thrombosis and Embolism, Allbutt's System of Medicine, 1899, vol. vii. p. 178.

² Archiv f. klin. Chirurgie, 1901, Band liii. Heft 3, p. 467.

³ Beiträge f. klin. Chirurgie, 1901, Band xxix. Heft 3, p. 545.

⁴ Deutsch. Zeitschrift f. Chir., 1901, Band lviii. p. 478.

⁵ Centralblatt f. med. Wissensch., 1876.

⁶ Archiv f. klin. Chirurgie, Band xxiii.

dition in the larger vessels of his cases of spontaneous gangrene, and considered the condition to be primary and the cause of the gangrene. Before Winiwarter, Billroth observed this obliteration of the larger vessels in some of his cases of spontaneous gangrene, and called the condition *endarteritis hypertrophica*. Winiwarter considered that the obliteration of the artery was due to a primary inflammation of the intima, producing a distinct obliterating intima growth and that a general arterio-sclerosis or a sclerosis of other coats of the affected vessel was not of necessity present. This view had been given acceptance by the majority of subsequent investigators. On the other hand, Zoege von Manteuffel¹ and his pupil E. Weiss,² from their pathological studies, have come to the conclusion that there is a primary arterio-sclerosis which may be of a very slight or a very marked degree, but that the occlusion of the vessel is due to the formation and organization of a thrombus, that is, these investigators consider that Winiwarter's obliterating intima growth is an organized thrombus. All authorities agree to the possibility of arterio-sclerosis in younger individuals which may go on to complete obliteration. Wulff, from a histological study³ of two cases observed in Israel's clinic in Berlin, comes to the conclusion similar to that of Zoege von Manteuffel. Bunge⁴ (and his results must be considered almost convincing) comes to a conclusion somewhat between the two opposing views. The study of his cases has demonstrated in every instance a basis of arterio-sclerosis as the primary condition. This sclerotic change may be diffuse, or there may be scattered discrete areas of sclerosis, rarely it may be solitary. This sclerosis produces a stenosis in one or more of the main vessels; it may extend to almost complete occlusion and endanger the life of the limb. As these areas of sclerosis are most frequently near the openings of the arterial branches the establishment of the necessary collateral circulation is frequently prevented. This impaired circulation, with the roughening of the intima coat, frequently leads to thrombosis, but it is the deposition and organization of the thrombus in every instance that produces the complete obstruction. Bunge cannot agree with Winiwarter that there is a specific disease—a primary *endarteritis obliterans*—nor can he agree with Zoege von Manteuffel that thrombosis occurs with very little arterio-sclerosis. Bunge's histological pictures lead him to state emphatically that one can distinguish between the picture of an intima growth and that of an organized thrombus. He suggests the term *arterio-sclerosis obliterans*.

¹ Archiv f. klin. Chir., 1891, and Deutsch. Zeitschrift f. Chirurgie, 1898.

² Deutsch. Zeitschrift f. Chir., 1894, Band xl.

³ Loc. cit.

⁴ Loc. cit.

THE CLINICAL PICTURE OF SPONTANEOUS GANGRENE IN YOUNG INDIVIDUALS. Charcot was first to describe the characteristic intermittent limping which is a very early symptom in patients who later (months or years) have spontaneous gangrene in the lower extremity, and in these individuals the vessel changes just described are always found. More recently Goldflam¹ and Erb² have called attention to the same symptom. Other symptoms noted by Bunge, Wulff, and Matanowitsch are numbness and coldness of the toes, foot, and even the leg, and the feeling of formication. When the peripheral pulse is felt it is very much weaker than on the other extremity, and later in the disease may disappear. The appearance of a gangrenous area or an ulceration on the extremity is an indication of complete obliteration of one of the larger vessels of the limb. Wulff's first case is a good example. The patient was a man, aged thirty-eight years. Without apparent cause for three years he suffered with intermittent attacks of pain in the leg and sensations of cold and formication. Two years ago an ulcer formed on the inner surface of the lower third of the leg. Although he gave no history of lues, he was given antisyphilitic treatment, but without benefit. Later it was noticed that the pulsation in the tibial vessels had ceased, and somewhat later also in the popliteal artery. At about this time the ulcer began to extend, the leg became colder, the pain increased, and then the pulse in the femoral artery disappeared. At the first examination in the clinic three years after the beginning of the pain, two years after the onset of the ulcer, the following was noted: The foot was ice-cold and blue; there was no arterial pulse in the limb; the ulcer had a slight gangrenous surface; the skin at the edge about the ulcer was indurated and the seat of eczema. The leg was amputated at the knee. The popliteal vessels (artery and vein) were thrombosed. The patient recovered, although there was some sloughing of the flaps. This demonstrates the truth of the conclusion in our discussion on diabetic gangrene, that the circulation of the stump is better when the popliteal artery is thrombosed after amputation in the lower thigh than at the knee.

Examination of the Specimen. The ulcer extended only to the muscles; the muscles were unchanged; the nerves were easily isolated and macroscopically were normal; the popliteal artery and its branches were thrombosed. Some of the smaller arteries were free. The microscopical study demonstrated that the nerves were unchanged, but both the open and obliterated arteries showed arterio-sclerosis, and the mass obliterating the arteries was considered by Wulff to be an organized thrombus.

¹ Deutsch. med. Wochenschrift, 1895.

² Zeitschrift f. Nervenheilkunde, 1898.

THE ETIOLOGY OF THE ARTERIO-SCLEROSIS, WHICH IS THE CAUSE OF SPONTANEOUS GANGRENE IN YOUNG INDIVIDUALS. On this subject we have not much data. Syphilis unquestionably in some of the cases is undoubtedly the cause. Haga,¹ in the study of fourteen cases in Japan, found a definite histological picture, which was first described by Virchow in 1858, and called luetic endarteritis. But Bunge's observation, also those of Winiwarter, Zoege von Manteuffel, and others, clearly indicate that the usual histological picture is distinctly different from the luetic endarteritis of Virchow and Haga. Clinically we cannot differentiate between the syphilitic and non-syphilitic form, which can only be settled by the microscopical examinations of sections of the diseased arteries.

Tobacco, alcohol, frequent exposure to cold, and trauma are considered by all authorities as factors in producing arterio-sclerotic changes in the young individual. Diabetes may be a cause.

THE TREATMENT OF SPONTANEOUS GANGRENE IN YOUNG INDIVIDUALS. So far it has been difficult to recognize the disease before the appearance of ulcers or gangrene. Even if we should recognize it in its earlier stages it is a question whether we could do much to prevent the ultimate result. Massage, elevation of the limb, supporting bandages, the avoidance of exposure to cold and trauma have been suggested. The appearance of pain in the lower extremities associated with a sensation of cold, intermittent limping, and formication should make us apprehensive of this disease, and a careful examination should be made of the pulse in the vessels of the limb. A smaller and a much weaker pulse would be another indication. Such patients should be given the benefit of the treatment just suggested, and also that of antisiphilitic drugs. I can find no cases in the literature in which the disease was recognized before the appearance of ulceration or gangrene.

After the appearance of gangrene or ulceration the surgical principles are clear. Infection should be prevented by proper measures, and operative interference should be guided by the same principles just discussed under diabetic gangrene, except in the absence of glycosuria a more conservative treatment may be followed. Unfortunately, in the large majority of the cases the larger arterial trunks are thrombosed and a higher amputation is usually necessary.

We have observed but two cases in Dr. Halsted's clinic. In one the patient was thirty-two years of age. The gangrene was of three weeks' duration, and had extended from the toe to the foot. It was necessary to amputate in the upper third of the leg. In the second patient, aged thirty years, the gangrene had been present two and a

¹ Virchow's Archiv., Band clii.

half months. Beginning with the toe, it extended to the middle third of the leg. On admission the gangrenous part had completely separated except the bone. The skin had sloughed, however, almost to the knee. We were able to save the upper third of the leg by skin-grafting the granulated surface.

SPONTANEOUS GANGRENE IN CHILDREN AND NEWBORN INFANTS. This is rare and usually due to congenital lues. Manatowitsch¹ reports two cases, one aged twelve years and one four weeks. In the girl, aged twelve years, the usual diseases, typhoid, malaria, and pneumonia, could be excluded as the cause. On first examination in the clinic, gangrene of the third, fourth, and fifth toe of the right foot was noted. It began in the fifth toe eight days before. For three weeks previous to the occurrence of this gangrene the child complained of pain and numbness in the right foot. The foot had been cyanotic. The pulse of the posterior tibial artery on this foot could not be palpated, while in the opposite foot it could be easily felt. It was necessary to remove the toes, and after a slow healing of the wound the patient recovered. The absence of the posterior tibial pulse was the only cause that could be made out to explain the gangrene; the patient, however, was very anæmic. A year and a half later she was readmitted with a similar condition in the fingers of the right hand, which rapidly extended to the right forearm. On admission the radial pulse was absent. In a few days the brachial pulse disappeared. It was necessary to amputate the forearm in the upper third above the line of demarcation. The patient died two years later of unknown cause.

Juvenile arterio-sclerosis had been described before by Hodgson in a girl, aged fifteen months, in the temporal artery; by Andral, in a girl, five years of age, in the aorta, and by Seitz, in three cases of young children, but none of these cases developed gangrene. Matanowitsch can find no similar case in the literature except one mentioned by Billroth, in his text-book, in which the autopsy showed nothing but grave anæmia. Matanowitsch's second case, in a child, four weeks old, was clearly due to hereditary syphilis. Krisowski² reports a case of symmetrical gangrene in an infant, confined to the ears, which he attributed to hereditary lues, and cured by antisypilitic treatment. Rachford reports a case of gangrene of both buttocks in a child, aged seven months, and Durante a case of gangrene of the entire lower leg in a child seven days old.

The possibility of gangrene due to malaria, although rare, should be constantly borne in mind.³

¹ Loc cit.

² Jahrbuch f. Kinderheilkunde, 1895.

³ PROGRESSIVE MEDICINE, December, 1900.

The possibility of any of these cases of gangrene being confused with Raynaud's disease is fully discussed by all these authorities. The clinical picture, however, and the pathological findings easily exclude this form of gangrene.

EXAMINATION OF THE BLOOD IN SURGICAL CASES.

Blood examinations of surgical patients are of sufficient importance to demand such an examination as a routine procedure. The grave anæmias, especially with hæmoglobin below 30 or 40 per cent., as discussed in *PROGRESSIVE MEDICINE* for December, 1900, contraindicate to a certain extent general narcosis. No careful surgeon should subject a patient to any operative interference except in emergency without a blood examination. In the presence of grave anæmia the operation, if possible, should be postponed until by proper treatment this condition has improved. Frequently we have to operate for various conditions in spite of the anæmia, and in some instances because the condition is the cause of the anæmia. In such cases, if feasible, the operation should be performed under local anæsthesia; if not, unusual precautions should be taken to curtail the amount and duration of the anæsthesia. That many patients recover from operations under general narcosis when they are suffering from severe anæmia is no indication that the condition is not a serious contraindication, because even the limited experience, in which we have careful blood counts, is sufficient evidence of the fact. In abdominal tumors, especially in the region of the spleen, no operation should be performed without a blood count. Leukæmia is a grave contraindication to operative procedure, and it has not been infrequent in surgery, and much to its discredit, that laparotomies have been performed for leukæmic splenic tumors. In cases of suspected hemorrhage the rise of the leucocytes is an early diagnostic sign. In a few hours the diminution in the red cells and hæmoglobin, especially if one has two counts showing this rapid change, is pathognomonic of hemorrhage. In typhoid fever, an infection not associated with a rise in the leucocytes, a leucocytosis is one of the most important diagnostic signs of a complication. In the various surgical infections and in the differential diagnosis of acute abdominal lesions the proper interpretation of the leucocyte count, especially when a number of counts are made, is an important aid in diagnosis. We have not sufficient data as yet to estimate the exact value of the leucocyte counts in the diagnosis of various surgical lesions.

If surgeons wish to be considered clinicians as well as operators, they must take advantage of the great advance that has been made in

the careful and systematic examination of the blood. At first sight, to those who have had experience with only a small number of counts in different surgical conditions, there appear to be too many exceptions to form a general working rule, and for this reason I fear that many surgeons have underestimated the value of the blood count. To interpret correctly the value of the blood count, especially the leucocyte count, it must be considered as one of the various symptoms, and it is of the utmost importance that it should be judged in relation to the duration of the other symptoms; for example, the leucocyte count is of value in the diagnosis of acute appendicitis when we interpret it with the duration and character of the attack. In typhoid perforations the rise of the leucocytes is of such short duration that, unless one has a record of the leucocyte count before, during, and after the perforation, the temporary rise might not be on record, and if clinicians did not make a leucocyte count until some hours after the beginning of the symptoms, they could truthfully say that in their cases of perforation they observed no leucocytosis. In the beginning and at the height of an attack of cholecystitis there is a rapid rising and a high leucocytosis, 18,000 to 30,000, with the disappearance of the acute symptoms, although the gall-bladder tumor may still persist; the leucocytes fall, and soon are very little, if at all, above normal, so that a leucocyte count in cases with symptoms of acute cholecystitis is a record of no value unless it is stated at what time after the beginning of the symptoms such count was made, and unless the symptoms at the time of the count are also recorded. The greatest variations in the counts are found in abscess formation, and for this reason quite a number of observers feel that the leucocyte count is of little value as an aid in the diagnosis of the collection of pus; a greater experience, however, will demonstrate the contrary. This will be fully discussed under appendicular abscess.

Very quickly after any obstruction of the intestine the number of leucocytes begins to rise; with onset of gangrene or peritonitis they rise for a few hours more rapidly and somewhat higher, but then begin to fall quite rapidly, so that if we simply record the single counts of cases of obstruction when first admitted to the hospital we will find the greatest variations, but when studied more critically we at once demonstrate that the variations are due to the duration and character of the lesion. When we are fortunate enough to have a great number of leucocyte counts in a single disease and, still better, a number of observations on each patient, and these are grouped according to the duration of the attack and the extent and character of the pathological lesion, the uniformity of the leucocyte counts becomes a rule rather than an exception.

Blood Examination in Traumatic Shock and Hemorrhage. This was fully discussed in *PROGRESSIVE MEDICINE* for December, 1900,

and little has been added in the literature on this subject except by a recent observer (I have mislaid the reference), who has demonstrated that immediately after a severe hemorrhage there is a temporary fall in leucocytes. The first change that we notice usually in one, two, or three hours is a rise in the leucocyte count from 15,000 to 24,000; the secondary anæmia as a rule does not show itself until five or six hours have elapsed. In cases of suspected internal hemorrhage a complete blood count should be made at once. If the symptoms have been present but an hour or two we would find only a leucocytosis. If a second count, made a few hours later, showed a diminution in the number of the red blood-cells and the hæmoglobin compared with the first count, this would be pathognomonic of hemorrhage, and the extent of the anæmia would be a slight index of the amount of blood lost. Such a record unquestionably would be of great value in the diagnosis of extra-uterine pregnancy with rupture and hemorrhage, but so far I can find no records in the literature. In cases of injury seen a number of hours after the accident the blood count would be a good index of the amount of hemorrhage. I can find no observations on the differential blood counts between shock from injury alone without loss of blood from that in which it is associated with hemorrhage.

The examination of blood after the contusion of the abdomen, to ascertain, if possible, whether we can distinguish by the change in the elements of blood the difference between shock from injury alone, internal hemorrhage, and peritonitis from rupture are not sufficient in number to allow any conclusions.

The Blood Changes Produced by General Narcosis. This was discussed in *PROGRESSIVE MEDICINE* for December, 1900, with reference to the statements of Mikulicz, Cabot, J. Chalmers Da Costa, and Fish, that a general narcotic was especially dangerous when the hæmoglobin was less than 50 per cent.

Before the American Surgical Association (May, 1901), J. Chalmers Da Costa and F. J. Kalteyer made a most important contribution to this subject.¹ The scanty literature of the subject is fully discussed. From their clinical examination and animal experiments they have clearly demonstrated that a general anæsthetic produces distinct blood changes, which in the normal individual is seldom if ever of any danger, and regeneration is rapid. In the anæmic individual these changes become serious, and they agree with the observations already made that an anæsthetic in patients with the hæmoglobin below 50 per cent. is a distinct danger, and should be considered a contraindication.

¹ Transactions of the American Surgical Association for 1901, p. 72, and *Annals of Surgery*, September, 1901, p. 229.

THE LEUCOCYTE COUNT AFTER AN ANÆSTHETIC. Da Costa and Kalteyer,¹ from an observation of fifty counts, found that the average leucocyte count previous to operation was about 9000, after operation about 14,000. In forty-three cases was this post-anæsthetic leucocytosis observed; in only nine instances the number was decreased after operation.

Cabot, Hubbard, and Blake, of Boston,² have studied the post-anæsthetic leucocyte count in fifty-seven cases. On the whole their conclusions agree with those of Da Costa and Kalteyer. In the majority of cases the increase in the leucocyte count was a relatively slight one, on an average not more than 20 per cent. (about 2000 to 5000); in five cases there was a decrease in the leucocytes; in a very few cases the leucocytosis was considerable; in ten cases in which their observation would allow them to estimate the duration of the post-operative leucocytosis it had disappeared within thirty-six hours after the time of the operation. Studied more in detail, the fifty-seven counts of Cabot, Hubbard, and Blake, it appears to me, allow even more deductions than they have made in their conclusions. There are forty cases in which the leucocyte count before the anæsthetic was given was 10,000 and lower, that is practically no leucocytosis. Among these forty cases, in thirty-seven a count was made after the ether but before the operation; with two exceptions the rise in the leucocytes is insignificant, usually only one, two, or three thousand, demonstrating that the increase in the number of white cells following the anæsthesia at this time is not sufficient to be of any importance. In one case the leucocytes rose from 10,000 to 16,000 after the anæsthetic; after the operation they still remained at 10,000; the operation was for stricture of the urethra. In the second case they rose from 8000 to 13,000; that is, in thirty-seven cases in which the leucocyte count before ether was 10,000 and less, after ether it was 16,000 in one case, 13,000 in one case, and 10,000 to 12,000 in thirteen cases. Among these forty cases, in thirty-six they have a record of leucocytes after operation; in eleven, or about 30 per cent., there was a distinct leucocytosis varying from 19,000 to 27,000, which, if there were further counts, usually disappeared in thirty-six hours. Judging from the character of the operation, this leucocytosis may be attributed more to the nature and extent of the operation than to the anæsthesia. In some there was slight hemorrhage, in others perhaps a slight infection; for example, in a case of operation for stone in the kidney the count before and after ether was about 7000, after operation on the same day 27,300, the next day 13,700, temperature 101°. In a case of empyema

¹ Loc. cit.

² Transactions of the American Surgical Association, 1901, p. 104, and Annals of Surgery, September, 1901, p. 361.

the leucocytes rose from 2800 before ether to 23,000 after operation. In a case of curettement of the uterus the leucocytes rose from 6000 to 19,000. In a case of hysterectomy in which there was some hemorrhage the leucocytes rose from 10,000 to 19,000. In a breast operation in which there may have been some hemorrhage or slight infection they rose from 6000 to 21,000. In one rather simple operation, the only one in this group, laparotomy and suspension of the uterus, they rose from 8000 to 24,000. Unfortunately in the majority of these eleven cases in which there was a distinct leucocytosis following the operation there are no further counts to indicate the ultimate course. It is sufficient, however, to demonstrate that a few hours after an operation of some duration and gravity, especially when there is any hemorrhage, we may expect in about 30 per cent. of cases a leucocytosis of 16,000 to 24,000. In my own experience this should fall in at least twenty-four hours to 16,000 and lower. In ten cases the leucocyte count before operation varied between 12,000 and 15,000. Of these cases we have eight counts directly after the anæsthetic. In one case there was a fall in leucocytes, 14,000 to 10,000, with no further rise after operation; in one case there was no change, but increasing 6000 after operation (15,000, 15,000, 21,000); in five cases the rise after ether was from 2000 to 6000, but in these cases after the operation the leucocytes remained the same in four cases; in only one was there a further increase of 300 (13,000, 15,000, 18,000). In only one case was there a marked increase in the leucocytes after the ether, 11,000, but in this case the leucocytes fell 4000 after the operation (14,000, 25,000, 21,000). In only three cases of this group were the leucocytes counted on the next day; in all they had fallen to 10,000, 12,000, and 15,000. In four cases the leucocytes before the operation varied from 17,000 to 20,000, after the anæsthetic the leucocytes in two cases fell slightly, but after operation rose slightly, falling again the next day. In two cases there was a slight rise in the leucocytes after the ether: in one case falling, in the other remaining the same after the operation.

Comparing this group of cases in which there was leucocytosis before the ether with the group in which there was no leucocytosis the change in the count after ether and after operation was about the same, except that we are dealing with higher figures.

Chadbourne¹ in an observation of twenty-one cases found the leucocytosis after the administration of ether most marked in the beginning of the administration.

Post-operative Leucocytosis. The value of the leucocyte count after operation is of course increased if we have a record of the count

¹ Philadelphia Medical Journal, February 18, 1899, p. 390.

just before operation and the evening after operation. On the whole, a rise in the leucocytes the evening after operation, unless very marked, is of no particular significance; but in complicated cases we should expect that within twenty-four hours the leucocytes will reach their normal figure. A continuing high and a rising leucocytosis is very suggestive of some complication. If there was no leucocytosis previous to operation it is almost pathognomonic. In cases associated with leucocytosis before operation, especially abscesses and infections, we should not expect the leucocytes to reach the normal limit for some time longer, two or three and sometimes four days. If after the fourth day the leucocytes still continue high, it is an indication that the infection has not been completely relieved.

C. Y. White¹ has contributed a most important article on the blood changes following *cœliotomy* in twenty-seven cases observed in Prof. Penrose's clinic in the University of Pennsylvania. The counts are especially valuable, because not only are there a number of complete blood counts before and a number of days after the operation, but a differential count of the white blood-cells, and in addition we have the correct diagnosis, the character of the operation, and the clinical notes after operation. White's conclusions agree with the statements already made. He has found that post-operative leucocytosis is constant, and its height seems to depend more on the severity of the operation than on the anæsthetic. The highest counts were found usually five hours after the operation. In cases drained with glass tubes the higher counts were later, within thirty hours. In the ordinary case the leucocyte count fell to normal on an average of five days, in drainage cases somewhat longer. Complications during the convalescence were always associated with an increase in the leucocyte count. In White's cases the higher post-operative leucocyte counts and its longer duration, I believe, are due to the fact that in the majority of his cases (fourteen) the operation was instituted for inflammatory conditions in the pelvis. In the majority of instances drainage was instituted. At such operations in the pelvis it is practically impossible to avoid the slight soiling of the general peritoneal cavity, following which one would expect an increase in the leucocytes, and on account of the infection which is always present along the drainage-tube we would also expect that the post-operative leucocytosis would be of longer duration. In the cases of Cabot, Hubbard, and Blake, this slightly higher and longer post-operative leucocytosis was observed after pelvic operations.

It is only with such excellent records as White's that we can estimate the true value of blood examination.

¹ University Medical Magazine, July, 1900, p. 260.

The Diagnostic Value of the Blood Count in Surgical Diseases.

It is first of importance to remember that in certain infections, for reasons which as yet we do not understand, there is an absence of leucocytosis.¹ The most important to be borne in mind by surgeons are typhoid fever, malaria, influenza (most cases), and tuberculousis.

Post-operative malaria is not an uncommon observation. In some cases the patients give no history of previous attacks; in the majority of cases there have been previous attacks, but in many instances there has been an apparently free interval of some months or even a year. Usually about twenty-four hours after operation there is a rapid rise in the temperature. The absence of leucocytosis is an indication against an infection; the finding of the malarial organism is pathognomonic, although in our own experience in some instances we have not found the organism until after a search of two or three days. Typhoid fever now and then is observed after operation, especially if in the wards both medical and surgical cases are treated. In a few cases in our own observation the absence of leucocytosis associated with a rising and continuous post-operative fever has suggested the possibility of the typhoid, confirmed later by the Widal reaction. It is not uncommon in the early days of typhoid fever to have abdominal symptoms suggestive of appendicitis. In such instances the leucocyte counts are of great value in diagnosis. Frequently tuberculosis presents symptoms of an acute pyogenic infection. If the inflammatory condition depends upon the tubercle bacillus alone there is no leucocytosis; if there is a secondary infection with pyogenic cocci a leucocytosis is usually present and is an indication for a more immediate operation.

Physiological Leucocytosis. According to Cabot we must bear in mind that the leucocytosis may be due to certain physiological conditions, and in such instances the estimation of the leucocyte count in the diagnosis of inflammatory conditions becomes somewhat more difficult, less so, if we are conversant with the normal physiological leucocytosis in this condition. In the presence of an acute inflammatory condition we would expect the leucocyte count to be much higher than that usually observed in such pathological lesions when the second factor (the physiological) was not present.

Physiological leucocytosis is observed in the (a) newborn, (b) after digestion, (c) during pregnancy and after parturition, (d) after violent exercise, massage, and cold baths, (e) there is also a leucocytosis in the moribund state.

LEUCOCYTOSIS IN THE NEWBORN AND IN CHILDREN. According to a number of observers a leucocytosis of 30,000 after a meal in children

¹ Cabot. *Clinical Examination of the Blood*, third edition, 1898.

up to two years of age should not be considered pathological. Head¹ lays special stress upon the presence of a greater number of leucocytes normally in children than in adult life. An increase, however, in the leucocyte count in children is associated with the same diseases as observed in the adult, with the exception that on account of the physiological leucocytosis the pathological is consequently higher; for example, Head observed no increased leucocytosis in measles, grip, or typhoid fever; but in appendicitis, osteomyelitis, scarlet fever, diphtheria, tonsillitis, and acute articular rheumatism, as in the adult, the increase in the leucocyte count is of great value in diagnosis and prognosis.²

DIGESTIVE LEUCOCYTOSIS is of chief value in the differential diagnosis in diseases of the stomach, and will not be considered here. On the whole, in the healthy individual after a full meal we should not expect a leucocyte count of more than 13,000 and perhaps 15,000, and it should also be remembered that total abstinence from food lowers the leucocyte count. This is of value frequently in acute abdominal lesions and in post-operative counts after laparotomy, in which during the observation of the patient very little food was given; for this reason a rise in the leucocyte count has special significance.

LEUCOCYTOSIS OF PREGNANCY. According to Cabot most primiparæ show a moderate leucocytosis during the latter months, 13,000 being the average. In multiparæ it is not so marked. In the last weeks of pregnancy it is not uncommon to notice a leucocytosis of 16,000 to 18,000. This physiological leucocytosis of pregnancy, especially in primiparæ, must be borne in mind in the diagnosis of complications arising during this stage of pregnancy. Biegonne³ and Ascoli and Esdra⁴ record a slight leucocytosis in the last few months of pregnancy.

THE LEUCOCYTE COUNTS DURING LABOR AND THE PUERPERIUM. The most complete article on this subject, with a discussion of the literature, has been published by Hibbard and White, of Boston.⁵ Here we have complete records of fifty-five cases. The counts before delivery varied from 7000 to 30,000. Taking 10,000 as the normal leucocyte count Hibbard and White found that the blood before delivery showed a leucocytosis in 84 per cent. of primipara and 75 per cent. of multipara. The average of the thirty-two primiparæ was about 15,000, and the average of the twenty multiparæ about 11,700. I have taken the liberty of making a table of my own from their table, with the follow-

¹ *Pediatrics*, February 1, 1900.

² *Brown's Review*, Maryland Medical Journal, March, 1901, p. 110.

³ *Archiv Russe de Path.*, etc., 1898, vi. p. 70.

⁴ *Bull. de la Soc. Lancisiana*, 1898, xvi.

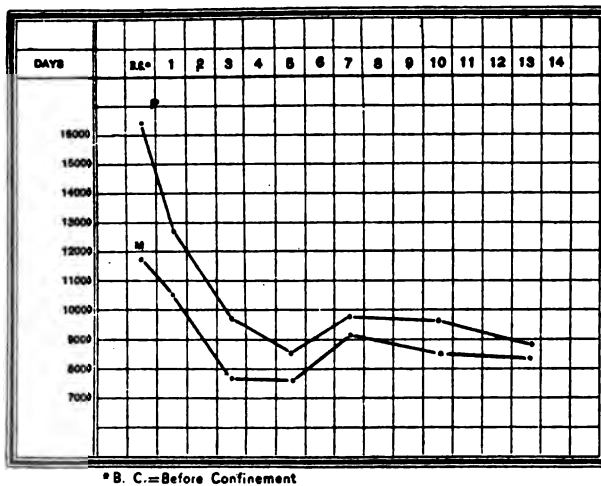
⁵ *Journal of Experimental Medicine*, 1898, vol. iii. p. 639.

ing results, showing the variation of the leucocyte counts before delivery :

Leucocyte count.	Primiparæ.	Multiparæ.
7-10,000	4	5
10-14,000	7	11
	—11	—16
14-20,000	14	2
20-30,000	5	1

This table demonstrates that the leucocyte count is rarely below 10,000, while in multipara it is usually between 11,000 and 14,000. In only one instance did they record a count of 20,000 ; this had fallen in forty-eight hours to 10,000, while in primipara counts up to 20,000 are not uncommon, and in five instances between 20,000 and 30,000. In only one of these six high counts did sepsis follow labor. A high

FIG. 14.
CHART A.



leucocyte count, therefore, at least in the primipara, even up to 30,000, is no indication that any serious complication will follow the labor.

The leucocytosis of normal convalescence is fairly characteristic. In twenty-two primiparæ and seventeen multiparæ the convalescence was normal and the average blood count in these cases shows a gradual fall, beginning on the first day after delivery and reaching normal on the fourth day, rising again slightly on the seventh day between 9000 and 10,000, then gradually falling again to normal. This is beautifully illustrated in Chart A (Fig. 14), which represents the average count in the normal cases at the different periods. My own table shows a slight exception, which is lost in the chart on account of taking the average, that is, in the nine cases whose leucocyte count before labor was from

7000 to 10,000 showed on the day after labor without an exception a slight rise in the leucocyte counts, and the fall to normal on the whole is slightly slower, that is, cases which have no leucocytosis before labor are more apt to show a slight leucocytosis after labor.

The Effect on Leucocyte Counts of Complications. Hemorrhage increases the leucocytosis to a slight extent. Mastitis: Hibbard and White observed but four cases, too few, I think, for definite conclusions. None of these cases went on to abscess formation, so we have no comparative leucocyte chart. In Case II. the leucocytes rose from 13,000 to 17,000 on the fifth day, and from 11,000 to 19,000 on the sixteenth day, in each instance associated with a rise of the temperature; in the first instance to 102°, in the second to 104°. In Case IV. the signs of inflammation were on the eighth and tenth days, the leucocytes rising from 7000 to 12,000 to 15,000. In Case XV. the leucocytes rose from 10,000 to 15,000, and in Case XXX. only from 9000 to 11,000. The highest leucocytosis associated with mastitis in these cases which did not go on to abscess formation was therefore 19,000. My own experience leads me to believe that a suppurative mastitis usually gives a leucocytosis between 20,000 and 30,000, and such a count even associated with slight local signs in the breast should be considered a positive indication for incision. Hibbard and White observed only three cases of slight sepsis; in one case no change in the leucocyte count, in two cases showing a rise of 14,000 to 17,000, and, as they write, these septic cases are too few to serve as a basis for any conclusion. In the one case of fatal eclampsia the leucocyte count before labor was 17,000, after labor it rose to 21,000. I should judge that in cases of severe infection following labor the leucocyte counts would be much higher twenty-four and forty-eight hours after labor. In Hibbard and White's table, with a few exceptions, the leucocytes fall from the beginning, and, as they state, in all but three of these cases there was no sepsis. The most rapid rise after labor (7000 to 17,000) was recorded in one of their cases of slight sepsis. In a recent observation of my own which I saw in consultation, on account of the possibility of a mastitis, the leucocyte count on the day after labor was 18,000. The patient was a young primipara, and this count could not be considered a high one; on the fourth day the leucocytes were 14,000; on the ninth day, associated with a rise of temperature and pain and tenderness in the left breast, the leucocytes rose to 30,000; an incision in the lower and outer quadrant demonstrated two small pockets of pus. Cultures from the breast tissue showed streptococcus and staphylococcus pyogenes aureus. In this instance the leucocyte count was an additional and important sign to indicate the early exploration.

As the general surgeon is not infrequently called in consultation for

complications during pregnancy and after labor, a familiarity with the normal leucocytosis of these conditions will, I think, be found to be of great value. Especially Chart A (Fig. 14), which I have reproduced, will indicate the normal leucocyte count of the various stages.

The leucocytoses after violent exercise, massage, and cold baths is so slight, seldom above 13,000, and of such short duration, that they need seldom be considered.¹

Terminal Leucocytosis. Cabot uses this term to designate the leucocytosis frequently observed in the moribund state. A few cases have been observed when just before death the leucocytes have risen rapidly from 7000 to 50,000 and higher. I have observed this in a few cases of patients dying from general peritonitis. In this infection in the early hours the leucocyte count is high, but it rapidly falls to 10,000 and lower. If the patient lives a day or more we frequently observe one or more high leucocyte counts. In death from various chronic diseases the terminal leucocytosis may be explained by the fact that frequently in these cases, as demonstrated by Flexner, there may be a terminal general infection.²

Pathological Leucocytosis. Cabot³ classifies these as follows: 1. Post-hemorrhagic leucocytosis; 2, inflammatory leucocytosis; 3, toxic leucocytosis; 4, leucocytosis in malignant disease; 5, leucocytosis due to therapeutical and experimental influences.

We have considered the post-hemorrhagic leucocytosis.

INFLAMMATORY LEUCOCYTOSIS. Cabot prefers this term rather than leucocytosis of infectious diseases, because as we have just stated there are a number of infectious diseases in which there is no leucocytosis. At the same time Cabot places under this heading some diseases in which inflammation plays but a very subordinate rôle. There are a number of factors which influence the leucocytosis in the inflammatory condition discussed by Cabot which I think for our purpose can be made more clear in the discussion of the leucocyte count of the various diseases. The resultant leucocyte count in the various infections is governed by a number of factors. Two are of quite importance: the severity of the infection and the resistance of the individual. Cabot expresses these factors in the following manner:

1. Infection mild.	Resistance good	= small leucocytosis.
2. " less mild.	" less good	= moderate leucocytosis.
3. " severe.	" good	= very marked leucocytosis.
4. " severe.	" poor	= no leucocytosis.

¹ Cabot, loc. cit.

² Statistical and Experimental Study of Terminal Infections, Journal of Experimental Medicine, 1896, vol. i., No. 3.

³ Loc. cit.

THE LEUCOCYTE COUNT IN ACUTE AND CHRONIC ABDOMINAL LESIONS.¹ On the whole the leucocyte counts in this field are of more interest and practical value to the surgeon than in any other, and in addition the records are more complete. The most interesting of the different abdominal lesions with regard to the leucocytosis is appendicitis.

J. C. Da Costa, Jr.'s, tabulation of 118 cases of appendicitis (Table I.) shows the range of the leucocytes :²

TABLE I.—LEUCOCYTES.

Leucocytes per c.mm.	Simple catarrhal and interstitial forms. (38 cases.)			Cases with abscess, gangrene, or general peritonitis. (80 cases)		
	Acute.	Chronic.	Total.	Acute.	Chronic.	Total.
Above 50,000	0	0	0	1	0	1
40,000-50,000	0	0	0	0	0	0
35,000-40,000	0	0	0	2	0	2
30,000-35,000	0	0	0	0	0	0
25,000-30,000	0	0	0	3	0	3
20,000-25,000	0	0	0	14	0	14
15,000-20,000	4	0	4	30	0	30
10,000-15,000	2	9	11	19	3	22
5,000-10,000	8	9	17	7	1	8
Below 5,000	4	2	6	0	0	0
Highest	17,100	15,000	17,100	58,500	14,600	58,500
Lowest	1,600	2,400	1,600	6,000	8,800	6,000
Average	9,124	9,190	9,158	17,718	12,425	17,453

Explanation of Table II. This table (see opposite page) represents all the counts made in cases of appendicitis. The first count in practically every instance was made when the patient was first admitted to the hospital, and this count is placed under the time corresponding to the number of hours or days since the beginning of the acute attack; subsequent counts (if made) are noted by dotted lines after the first count under the proper time. In the cases operated upon the last count represents the time of the operation, with one exception, in the group *appendicitis, general peritonitis, operation*. The letters Op. under the figures 20 represent the time of operation. The three subsequent counts are post-operative, and show the fall in the leucocytes, with general peritonitis. Under the column *appendicitis, abscess, operation*, there are only single counts. The figures 2 or 3 in front of the figures representing the number of leucocytes indicate that there were two or three cases with this number of leucocytes at this time. Under the column *appendicitis, general peritonitis, operation*, the letter R indicates the patient recovered,

¹ In the discussion of this subject I have drawn largely from my paper read before the American Surgical Association in May, 1901, published in its Transactions, the Medical News, August 31, 1901, and the Maryland Medical Journal, September, 1901, and from the more complete article to be published in the Annals of Surgery for December, 1901.

² Transactions of the American Surgical Association, May, 1901, p. 68.

and D the patient dead. The time in these cases represents the entire interval of the acute attack, and not the duration of the peritonitis, which, in the majority of cases, was impossible to ascertain.

TABLE II.—BLOODGOOD'S TABULATION OF THE LEUCOCYTE COUNTS IN APPENDICITIS OBSERVED IN THE SURGICAL CLINIC OF PROF. HALSTED, OF THE JOHNS HOPKINS HOSPITAL.¹

Hours.								Days.					Weeks.		Months.
6 to 14	16	20	24	30	36	40	48	II. to III.	III. to IV.	IV. to V.	V. to VI.	VI. to VII.	1 to 2	2 to 4	1
Chronic and subacute appendicitis.															
								10	12	10	7		6	4	5
					15			10	6	15			6	6	6 (2)
								18					7	8	7 (2)
								15		15	14		8	10	10 (5)
													9	11	11 (8)
															12
Acute appendicitis. Operation. Recovery.															
	14	12						17	12	9		14	9	12	8
17	13							11						7	
22	16							11	8	7	6				
Acute diffuse appendicitis. Operation. Recovery.															
8	11	17	18					11	9			9		12	10
17	10	7	13	17								14	10		15
	12	17													
	13	25													
Gangrenous appendicitis. Operation. Recovery.															
13	16	17	17	35				21	16			13	20	17	
	13	28	25					14	20	17					
Acute appendicitis, distended with pus. Operation. Recovery.															
	15							17	20	18	24	35	(5 hours)		
	19							21	28						
Appendicitis. Abscess. Operation.															
	11							11	11	12	12	11	8	6	(2)
	18							19	20	16	24	12	14	7	9
	27	30	32					22	26	16	26	14	17	(2)	8
								27	30		29	15	(2)	18	(2)
												18	(2)	19	(2)
												19	(2)	25	(2)
												25		60	
												27		19	
												30		20	
														28	(2)
Appendicitis. General peritonitis. Operation.															
14R	32D	36R	25D					11D	21D	14R		15D	14D		
								11D	24D	15D					
8		20	23	26			11D	13D	35D	29D					
		Op.						14D	40D						
			30R					17R							

CHRONIC AND SUBACUTE APPENDICITIS. In my table there are thirty counts, and in this group there are included all those cases of appendicitis first admitted at the end of the attack or in the quiescent

¹ A few cases have been added since the first publication.

period after one or more attacks. All these cases were operated upon. The appendix showed acute inflammation in various stages, but there was no pus. In twenty-four cases the leucocyte count was below 12,000. In five cases between 12,000 and 15,000. These findings correspond exactly with a similar group in J. C. Da Costa, Jr.'s, cases, the chronic catarrhal or interstitial appendicitis. In Da Costa's twenty counts the highest was 15,000. In my own cases the higher counts, 12,000 to 15,000, were observed in cases admitted at the end of the attack presenting still some slight symptoms. If a further count was made in these cases before operation the number of leucocytes fell. In one of our cases the leucocyte count was 18,000, but in addition to the chronic diffuse appendicitis there was partial intestinal obstruction from adhesions, explaining the higher count. These fifty counts of Da Costa's and my own give us a very accurate basis for our interpretation of the number of white cells in chronic and subacute appendicitis not associated with pus. The differential diagnosis from cases of appendicular abscess will be considered later.

ACUTE APPENDICITIS. In my table I make two groups: cases admitted during the acute attack which were not operated on, in which we only can infer the condition of the appendix, and cases which were operated upon and an acute diffuse appendicitis found. Da Costa groups his eighteen counts under the column: acute catarrhal appendicitis. His highest count was 17,100, average count 9124, corresponding closely with the counts in my table. In this group of acute diffuse appendicitis we should not expect very high counts, because either very shortly after the first observation the attack has rapidly subsided, with a fall in the counts, or we have operated before the onset of gangrene, abscess, or peritonitis, unquestionably the better time if possible for operation in every case of acute appendicitis. In the cases not operated on we have observed in every instance a fall in the leucocytosis associated with subsiding local conditions. The highest count in our own observation was 22,000. This patient was admitted twenty hours after the beginning of the acute attack with a leucocytosis of 22,000. The clinical symptoms, however, were not marked; observed eight hours the leucocytes fell to 16,000 and the local symptoms practically disappeared. Within the next twenty-four hours the leucocytes had fallen to 11,000 and by the fifth day to 6000 (see Table II.). Although this patient with a leucocytosis of 22,000 at the end of twenty hours recovered, and there is every reason to believe that the inflammatory condition about the appendix subsided, nevertheless, it is an exception to the general rule, and it would be safer, I believe, to operate in these cases, even if the symptoms of appendicitis are slight, if the leucocytosis rises to 20,000 within the first forty-eight hours. In two cases

the leucocytes were 17,000. One, first observed sixteen hours after the beginning of the attack, falling to 13,000, and then to 11,000 within forty-eight hours. The other, observed forty-eight hours after the beginning of the attack, falling quickly to 12,000. In the other cases the leucocyte counts were lower. In the cases of acute diffuse appendicitis operated upon, the leucocyte counts do not differ much from those not operated upon, except, if observed, we found a rising leucocytosis. In a few cases a falling leucocytosis. In this group we have observed but one count above 20,000, and in this instance the exudate about the appendix was much more excessive. I observed this patient thirty-six hours after the beginning of the attack. Clinically the local signs had subsided, the temperature had fallen from 102° to 100° . The operation was performed at once on account of a leucocyte count of 25,000, because in the majority of instances such a high leucocytosis within forty-eight hours after the beginning of the attack has been associated with a gangrenous appendix, an appendix distended with pus, an abscess or beginning general peritonitis. From a study of these cases we might formulate the following rules: If a patient, first observed within forty-eight hours after the beginning of the attack, has a leucocytosis of 18,000 or more, this should be considered a justifiable indication for immediate operation, whether the symptoms are slight and subsiding or not. If the patients are observed from the early hours of the attack a rapid rise in the leucocyte count up to 18,000 is a sufficient indication for immediate operation, irrespective of the acuteness of the local symptoms. In cases observed in which the leucocytes fall, but the local signs increase in severity, we should operate in spite of the falling and low leucocyte count. Cases of appendicitis, first observed after forty-eight hours, in which the local signs have subsided, and in which the leucocytosis is 15,000 or lower, can be allowed to wait for further observation. If the leucocytes fall we can feel quite satisfied that it is simple diffuse appendicitis (catarrhal appendicitis), and the probabilities are that they will recover from this attack.

If, on the other hand (especially if the patient is under proper treatment), the leucocytes begin to rise, we have an indication for operation, in spite of the local symptoms. This rise of the leucocytes is very suggestive of abscess formation.

Da Costa, in his table, has grouped gangrenous appendicitis, abscess, and peritonitis together. This is unfortunate, because abscess and peritonitis give such a diversity of counts, according to the duration of the disease and its extent. However, his table shows the uniformly higher counts in this class of cases. In my table I have found it much more satisfactory for study to make four groups.

GANGRENOUS APPENDICITIS. OPERATION. RECOVERY. We notice at once the higher counts, in the majority of instances over 20,000, and in cases observed from early in the attack a very rapid rise in the leucocyte count. In one instance the rising and high leucocytosis was the chief factor on which the diagnosis was made, and the early exploratory operation was instituted. The case seems of sufficient importance to be reported in detail.

Case I.,¹ observed by Dr. Thomas R. Brown, of Baltimore, communicated to me personally, is perhaps the most important. The patient, a boy, aged eleven years, indulged freely one Saturday night about 8 o'clock in strawberry ice-cream and soda water; at 4 o'clock the next morning he was awakened by severe epigastric colic, nausea, and vomiting. The patient was seen by Dr. Brown at 8 A.M. (four hours); temperature 98° F., pulse 76. He was given a Seidlitz powder and powders of subnitrate of bismuth. The abdominal examination was negative. He was seen again at 10 A.M. (six hours); no change in the symptoms; no nausea or vomiting. At 6 P.M. (fourteen hours) the temperature was 98.8° F., pulse 86. There had been a stool; the urine was voided without pain; he was apparently very comfortable, and complained of no pain; abdominal palpation was negative; he looked, however, a little languid. There was nothing in the clinical picture to suggest that the condition was anything more than that to be explained by indigestion. On Monday morning at 8 o'clock (twenty-eight hours after the attack of colic) his temperature was 99.4°, pulse 95. He had passed a comfortable night; no nausea or vomiting; no abdominal symptoms, but he looked a little more depressed. The leucocyte count at this time was 17,000. (A leucocytosis twenty-eight hours after an attack of abdominal colic in a patient taking practically no food is an indication of some inflammatory condition.) At 11 o'clock the leucocyte count was 17,500, temperature 100° F., pulse 100, but no abdominal signs. At 4 o'clock (thirty-six hours after the beginning of the colic) the leucocyte count was 35,000, temperature 100.6° F., pulse 100. For the first time in the right iliac fossa there seemed to be a little swelling; no marked muscle spasm nor tenderness. He did not complain of pain when he voided urine. This rapid and high rise in leucocytes, even without abdominal symptoms, but following abdominal colic, was considered by Dr. Brown, his physician, and Dr. Finney, the consulting surgeon, a sufficient indication for exploration of the abdomen. On opening the abdomen an appendix eight inches in length and extending into the pelvis was found. The appendix was gangrenous for at least two-thirds of its length, and perforated at its tip;

¹ Bloodgood, Medical News, August 31, 1901.

no adhesion, and no localization. The pelvis was filled with cloudy fluid; the intestines in the pelvis and right iliac fossa were injected, covered with a little fibrous exudate and cloudy fluid. Cultures were not taken. The patient recovered.

In this case the rise in the leucocytes was practically the only indication for operation. There were no previous attacks of appendicitis, and the only clinical manifestations pointing to the appendix was the onset of the abdominal colic associated with nausea and vomiting.

ACUTE APPENDICITIS DISTENDED WITH PUS. The clinical signs and the leucocyte counts in this group of cases correspond very closely with those in gangrenous appendicitis. It will be noted that among ten cases of gangrenous appendicitis there are three cases with leucocyte counts below 18,000. In one case, observed twenty hours after the beginning of the attack, although the leucocyte count was but 17,000, the history and clinical picture were typical and the patient's condition was sufficiently critical to warrant immediate operation. The two other cases admitted on the third and the fifth day with a leucocyte count of 16,000 and 13,000, had but small areas of gangrene.

ACUTE APPENDICITIS. ABSCESS. We have observed an abscess from acute appendicitis in but three instances before the beginning of the third day of the attack, in one twenty hours after the beginning of the attack the leucocyte count was 18,000, in the second case, first observed twenty-four hours after the beginning of the attack and not operated on for twelve hours, the leucocyte count was 27,000, rising to 32,000; I cannot explain the low leucocyte count, 11,000, in the third case, observed twenty-four hours after the beginning of the attack, except that the abscess had been there for a much longer period. There was a history of recurrent attacks at rather short intervals. The adhesions about the appendix and the small collection of pus indicating a process of much longer duration.

CASES OF APPENDICULAR ABSCESS WITH LEUCOCYTE COUNTS BETWEEN 6000 AND 12,000. Da Costa records thirty counts, or 37.5 per cent., below 15,000. In my table there are fourteen cases with leucocyte counts between 6000 and 12,000, about 26 per cent. The duration of the attack in these cases varied from two days to one month and over. This demonstrates that we may have a localized abscess in appendicitis with no leucocytosis. Studying these cases more carefully, clinically we find that in eleven out of fourteen cases the patients were practically at the end of the acute attack; in eight of these eleven cases there were no local symptoms except tumor; the highest temperature was 101°, average temperature about 99°. Clinically, therefore, these eight cases of abscess could be differentiated from chronic and subacute diffuse appendicitis only by the presence of a palpable tumor. The

remaining three cases of the eight of chronic abscess with leucocyte counts below 12,000, in two there were slight local symptoms in addition to tumor, in one there was neither local symptoms nor tumor; in this case the last attack had been one month previous to admission.

Of fourteen cases of abscess with leucocyte counts below 12,000, in only three were the local symptoms acute; one, observed twenty-four hours after the beginning of the attack, has been discussed; a second patient was very ill and died after the incision of the abscess; the low count may be explained by the extreme septic condition or the general peritonitis; the third patient was also very ill; there was a huge pelvic abscess; duration of illness two and one-half days; there was no general peritonitis, and the patient recovered.

CASES OF APPENDICULAR ABSCESS WITH LEUCOCYTE COUNTS BETWEEN 12,000 AND 15,000. Nine cases: in eight the symptoms were subacute or absent, except in every instance there was a distinct, palpable tumor; in only one case were the local symptoms acute; the patient was admitted on the sixth day; the leucocyte count was 14,700; and on palpation of the abdomen a tumor could not be made out.

CASES OF APPENDICULAR ABSCESS WITH LEUCOCYTE COUNTS BETWEEN 15,000 AND 60,000, 63 PER CENT. Of these, nineteen were above 20,000, in the greater majority 18,000 and more. From these figures we can conclude: In cases of appendicitis within forty-eight hours from the beginning of the attack an abscess with one exception has been associated with leucocytosis above 18,000. The majority of cases of abscess are observed after the second and third day. If the local symptoms are acute, with the rarest exception, we observe a leucocytosis above 18,000. In cases in which the symptoms are subacute or have subsided, as a rule the leucocyte count is above 15,000, differentiating the case at once from chronic and subacute diffuse appendicitis; but in a number of instances we have observed leucocyte counts between 6000 and 15,000, but in these cases, unfortunately, there has been but a single count, and I am very much inclined to believe that if further counts had been made we would have found a leucocytosis above 15,000 in almost every case of abscess. I am forced to this conclusion from the record of successive counts in other cases. Among the cases of abscess with leucocyte counts above 15,000, the leucocyte count on admission has been 12,000 and lower. If they had been operated on at this time the case would have been recorded among those of abscess with leucocyte counts of 12,000 and lower, but on observation further counts have demonstrated a rise in the leucocytosis. We have also observed cases of abscess admitted with a high leucocytosis to show a fall, and if further observed a rise. From these observations I believe that chronic and subacute appendicular abscess can be

differentiated from chronic and subacute appendicitis by the distinct fluctuation in the leucocyte counts. We need further observations on this point.

ACUTE APPENDICITIS. GENERAL PERITONITIS. OPERATION. The correct interpretation of the leucocyte count in this group of cases is difficult, because in the majority of cases it is hard to estimate the duration of the peritonitis. Observation seems to demonstrate that in the early hours of peritonitis there is a rapid rise in the leucocytes, which, however, soon falls. These cases have been grouped according to the duration of the attack, and not to the approximate duration of the peritonitis. Five cases have been observed, in each of which the beginning of the attack was within forty-eight hours. Three cases recovered—one, operated on sixteen hours after the beginning of the attack, with a leucocytosis of 14,000; one, twenty-four hours, with a leucocytosis of 32,000; and one, thirty-six hours, with a leucocytosis of 36,000. In these three cases there were distinct local symptoms, but slight general abdominal symptoms. There was no distention of the intestine; the exudate was chiefly purulent; in the exudate in the general peritoneal cavity only the colon bacilli were found, and no streptococci. In one case, observed forty-eight hours after the beginning of the attack, and operated on at once, the leucocyte count was 25,000. The general abdominal symptoms masked the local symptoms, the patient was very ill, the intestines were distended, streptococci were present, and the patient died. One patient was observed in the hospital. Twenty hours after the beginning of slight abdominal colic, localized in the right iliac fossa, the leucocytes were 8000; six hours later, or thirty-six hours after the beginning of the attack, the leucocytes were 20,000. Clinically, the patient was not very ill, but on account of the rise of the leucocytes from 8000 to 20,000 operation was performed. The appendix was perforated and surrounded by a few drachms of purulent material. This pus was not walled off by adhesions; the general peritoneum was slightly infected; it appeared as if there were beginning general peritonitis. After the operation the leucocytes continued to rise for twelve hours up to 26,000; then within the next twelve hours fell to 11,000, the patient dying with a clinical picture of peritonitis, which was found at autopsy. In this case the streptococci were present. In five cases admitted three days after the onset of the symptoms, all showing the clinical picture of peritonitis, the leucocyte counts in four were 11,000, 11,000, 13,000, and 14,000. These four cases were fatal. The fifth case, whose leucocyte count was highest (17,000), recovered. The cultures from the peritoneal cavity in this case showed bacillus coli communis. These counts seem to demonstrate that within forty-eight hours after the beginning of an

attack a very high leucocytosis is suggestive—but not at all positive—of beginning peritonitis, and that the leucocyte count does not help us with regard to prognosis. After the second day, in cases in which the peritonitis has been present longer, we have never observed a recovery with a low leucocyte count. If the leucocytosis still remains high at this period the prognosis seems better for the ultimate recovery after operation.

CONCLUSIONS IN REGARD TO THE INTERPRETATION OF THE LEUCOCYTE COUNT IN APPENDICITIS. Perhaps in the majority of instances we can easily make the diagnosis as to operative intervention by the local symptoms. This is especially true when the local symptoms are very acute. Here one should operate irrespective of the leucocyte count. On the other hand, in cases of appendicitis in which the local symptoms are less marked, or, in a few instances, hardly sufficient to make a positive diagnosis, every additional experience has demonstrated the value of the leucocyte count. Within the first forty-eight hours a leucocytosis of 18,000 should be considered an indication for operative intervention, especially when we have observed the case from the beginning and have recorded a rising leucocytosis. With the rarest exceptions a leucocytosis of 18,000 has been associated with excessive exudate about the diffuse appendicitis, gangrene, or an appendix distended with pus, abscess, or general peritonitis. When the leucocytes are below 18,000, and the symptoms have subsided and further counts demonstrate a fall, with hardly an exception this is an indication that the patient is recovering from the attack.

First observed between the third and seventh day, a leucocytosis of 18,000 in the majority of instances is an indication for immediate operation. In a few cases in which the local symptoms: muscle spasm, pain and tenderness are subsiding or have ceased, and we find on abdominal palpation a distinct tumor, and when these facts are associated with a good general condition of the patient we may delay the operation, because in the great majority of instances we are dealing with a localized abscess. The experience in these cases seems to indicate that proper delay, with rest and careful dietetic treatment, decreases the danger of the operation, especially peritonitis from infection of the peritoneal cavity during the manipulation of opening and draining the abscess. The delay also increases the probability of the removal of the appendix without additional risks when the abscess is opened. Such patients should be carefully observed, any increase in the local symptoms or a sudden and high rise in the leucocytes indicate an extension of the purulent process, and is an indication for immediate operation.

After the seventh day the differential diagnosis, with very few exceptions, lies between chronic and subacute diffuse appendicitis and

abscess. Here the leucocyte count is of great value and has been fully discussed.

Leucocytosis in Intestinal Obstruction. Cabot¹ has very little to say about the leucocyte counts in intestinal obstruction, except that the white cells may be increased, especially when the obstruction is cancer. Dr. Harvey Cushing, I think, was the first to call attention to the leucocytosis associated with intestinal obstruction.² I have previously referred to this in the observations on strangulated hernia.³ Since Cushing's first count in August, 1898, the leucocytes have been estimated in almost every case of intestinal obstruction observed in the surgical clinic of the Johns Hopkins Hospital and in a number of outside cases. The great uniformity of the records have placed the leucocyte count as one of the most important factors in the diagnosis of obstruction. From a large number of observations (to be published in the *Annals of Surgery*, December, 1901) the following conclusions can be made: Within a few hours after the beginning of the obstruction there is a rapid rise in the leucocyte count; within the first twenty-four hours, if complete, usually 20,000; if partial, 14,000 to 16,000. If gangrene of the obstructed loop or peritonitis take place within the first twenty-four hours the leucocyte count is usually higher, 25,000 to 30,000. On the second day the leucocyte counts in both conditions are about the same. After this time, if gangrene or peritonitis is present, the leucocytes begin to fall, but in the absence of such a complication the count remains high. After three or four days in complete obstruction without gangrene or peritonitis the number of leucocytes begins to fall, associated with symptoms of auto-intoxication. In cases of obstruction of the intestine, with a history of more than three days' duration, the leucocyte count above 20,000 is a good prognosis, below 20,000, and especially if below 15,000, the probabilities are that gangrene or peritonitis are present or that the patient is very much poisoned by auto-infections. A high leucocytosis without fever and associated even with very slight symptoms of obstruction is an indication for operation. In post-operative complications suggestive of obstruction the leucocyte count is of great value in the diagnosis.

The Leucocyte Count in Cholecystitis and in Abscess, Cirrhosis, and Carcinoma of the Liver.⁴ On this subject there is very little in the literature.⁵ From my own observations the following conclusions

¹ Loc. cit.

² Laparotomy for Intestinal Perforation in Typhoid Fever, Johns Hopkins Hospital Bulletin, November, 1898.

³ Johns Hopkins Hospital Reports, 1898, vol. vii. p. 332.

⁴ Complete report to be published in the *Annals of Surgery*, December, 1901.

⁵ See Brown's Review on the Pathology of the Blood, Maryland Medical Journal for December, 1900, etc.

can be made: In acute cholecystitis the leucocytes invariably rise to from 20,000 to 27,000. If the patients are not operated on at the height of the attack the leucocytes fall coincident with the disappearance of the local symptoms, although the gall-bladder tumor may still persist. Thayer¹ reports two cases of acute cholecystitis during typhoid fever. In both there was a rising leucocytosis associated with local symptoms in the gall-bladder area. In chronic cholecystitis, irrespective of the condition or bacteriology of the gall-bladder, the leucocyte counts in eight cases varied between 5000 and 12,000. In cholecystitis associated with jaundice and stone in the common duct, the leucocyte counts in eight cases have varied from 2500 to 10,000, irrespective of the duration of the jaundice. One patient observed from the beginning of the acute attack showed a rising leucocytosis to 24,000; after the acute local symptoms had subsided the leucocyte count fell to 9000, but the jaundice persisted, and at the operation a stone was found in the common duct. In cirrhosis of the liver, even with jaundice, there is, as a rule, no leucocytosis. In abscess of the liver the leucocytosis is higher than in acute cholecystitis, usually above 30,000, in one case 85,000. In carcinoma of the liver, with or without jaundice, the leucocyte counts varied; in four cases below 8000, in three cases high (17,000, 44,000 and 70,000). These cases with high counts were observed by Dr. James F. Mitchell, who will soon make a complete report. Cabot² also calls attention to the high leucocytosis in cancer of the liver. He records nineteen counts, the highest 35,000; in seven cases below 10,000; of the others the majority between 15,000 and 25,000. Cabot has also observed that in cancer of the liver there is frequently a daily fluctuation in the number of the leucocytes, but with no particular regularity, one case fluctuating between 10,000 and 28,000 during a period of two weeks. Mitchell's case also showed this fluctuation. In regard to abscess of the liver, Cabot writes: In all but one of the cases the leucocytosis has been very marked, and I have never been able to account for its absence in this case. We have also observed fluctuation of the leucocyte counts in abscess of the liver. The highest count recorded by Cabot in abscess of the liver was 48,000.

CONCLUSIONS. In cases with acute symptoms, referred to the gall-bladder or liver, leucocytosis is associated with acute cholecystitis, abscess, and carcinoma. If the count is above 30,000 it is in favor of abscess or carcinoma. In cases with no acute local symptoms a leucocytosis is almost pathognomonic of abscess or cancer. Extreme fluctuation in the count and absence of fever are in favor of cancer.

¹ Observations on the Blood in Typhoid Fever, Johns Hopkins Hospital Reports, 1900, vol. viii.

² Loc. cit.

In cirrhosis of the liver without jaundice, Cabot reports but one high leucocyte count (16,000) and associated with hemorrhage. In five cases of cirrhosis with jaundice there are two counts of 19,000, all lower counts, as a rule, than in the other diseases of the gall-bladder and liver associated with leucocytosis.

The Leucocyte Counts in Acute Hemorrhagic and Suppurative Pancreatitis. On this subject I can find nothing in the literature. Cabot does not mention it. In the extensive recent literature on the surgery of the pancreas, blood counts are not recorded. In acute hemorrhagic pancreatitis the loss of blood is hardly sufficient to produce a secondary anæmia. There might, however, be a slight leucocytosis. I have observed one case of suppurative pancreatitis with a leucocytosis of 19,000.¹

Leucocyte Counts in Diseases of the Kidney. On this subject there is also very little in the literature. I could find nothing in Brown's review.² In the acute symptoms of renal colic from calculus there is no leucocytosis. This has been so in the few cases which I have observed. Its absence is an aid in the differential diagnosis from appendicitis and infections of the kidney. Cabot has observed a slight leucocytosis in a few cases of acute and chronic nephritis which, he believes, is due to either uræmia or hemorrhage. In six cases of floating kidney reported by Cabot there was no leucocytosis. In renal colic from stone in the kidney Cabot records a leucocytosis only in those cases in which there was an infection. In five cases of my own observation of acute infection of the kidney, in two associated with congenital cysts the leucocyte counts were between 25,000 and 30,000. We have as yet no records of any extent of blood counts in chronic pyelitis and pyonephrosis. Careful counts in cases of enlarged prostate and cystitis might aid us in the recognition of a pus-kidney. If this is found to be true it would be the greatest aid in regard to operative and non-operative interference in these cases. The chief mortality in operations for these diseases is due to the advanced disease of the kidney, usually pyelitis and pyonephrosis, conditions almost impossible to recognize clinically, and catheterization of the ureters is always difficult and dangerous on account of the size of the prostate and the necessary narcosis.

The Leucocyte Counts in Acute and Chronic Conditions of the Tube and Ovaries. The careful study of numerous observations of the leucocyte counts in the early hours and days of acute salpingitis might be of great interest and value in the differential diagnosis from appendicitis, because in salpingitis experience is against early operation,

¹ Johns Hopkins Hospital Bulletin, January, 1901, p. 26.

² Loc. cit.

because in many instances the infection takes care of itself, there is very little danger of peritonitis, and if suppuration takes place the best results are obtained by an incision of the abscess through the vagina.

Cabot has recorded fifty-one counts in pelvic abscess. The duration of the disease in these cases is not given. On the whole, the leucocyte count corresponds very much with that in appendicular abscess.

The Leucocyte Counts in Abdominal Tumors. In benign tumors and sarcoma without acute obstruction there is no leucocytosis. In carcinoma, especially if there is metastasis to the peritoneum and mesentery glands, we not infrequently observe leucocytosis. Cabot records this, and we have observed it in our own cases. The count is usually between 15,000 and 20,000, much lower than in cases of primary and secondary carcinoma of the liver.

The Leucocyte Counts in Tubercular Peritonitis. Frequently this condition is associated with acute abdominal symptoms. If there is no obstruction and no abscess from a secondary pyogenic infection the leucocyte count is low, even in cases with high temperature and marked abdominal symptoms. Cabot records twenty-eight counts. In twenty-four cases the leucocytes varied from 2000 to 8000; in three cases from 10,000 to 11,000; in one case the leucocytes associated with pelvic abscess the leucocytes rose from 16,000 to 18,000. Cabot's observations correspond with those of our own. We have observed a leucocytosis in only two cases, both associated with obstruction: one of 15,000, observed forty-eight hours after the beginning of the symptoms, and one with 17,000 observed eight hours after the beginning of the symptoms, both lower counts than usually observed in obstructions not associated with tubercular peritonitis.

CONCLUSIONS. Sufficient space has been taken to demonstrate the value of blood examinations in various surgical conditions, I trust, to stimulate others to aid in carrying on further investigations.

That clinical microscopy has taken a very important place in surgery is evident from the fact that the New York State Medical Society and the American Surgical Association each devoted a day to a symposium on the blood at their respective annual meetings of this year, and Dr. John A. Wyeth took for the subject of his oration on surgery, delivered before the American Surgical Association, "The Value of Clinical Microscopy, Bacteriology, and Chemistry in Surgical Practice."¹

I believe few in the profession will agree with the following statement made by Dr. John B. Deaver before the American Surgical Association:² "In the last few years there has crept into the profes-

¹ American Medicine, June 8, 1901, p. 445.

² Transactions of the American Surgical Association for 1901, p. 115.

sion a tendency to replace the bedside by the laboratory as the point from which to make the diagnosis ; to substitute the highly magnified but extremely limited field of the microscope for the broader view of the eye of the physician. This we regret, for in the majority of instances the diagnosis must be made at the bedside without the aid of the microscopist, and any man who has no confidence in diagnosis made without the aid of the laboratory limits his usefulness."

The facts are in favor of the directly opposite of this view. The great development in recent years in the improvement of bedside diagnosis is due to the aid of laboratory investigation. The student and clinician who in his training has associated all his bedside study with careful laboratory examination more completely recognizes and interprets the very earliest symptoms and signs of the disease, and with this training he is far better able to recognize similar conditions in their early and more or less obscure stages when he is in a position in which laboratory aid is inconvenient or impossible. The ability to recognize pathological conditions by their naked eye appearances at the operation and on the autopsy table is only developed by the comparative study of the gross and microscopical examinations, and the time soon comes after such a study when the gross diagnosis is seldom at fault, and the microscope can be used simply in confirmation.

DISEASES OF THE KIDNEYS.

By JOHN ROSE BRADFORD, M.D., F.R.C.P.

OXALURIA.

SOME of the constituents of the urine present in disease derive their importance either from the quantities present or from some slight abnormality in the mode of their excretion. Other urinary substances are important, owing to the fact that their presence in the urine throws some light on the metabolic processes in the body. In a few instances certain urinary constituents may be of importance from all these three different points of view, and this is notably so in the case of uric acid. An increase in the amount of uric acid excreted in the urine may not only give rise to urinary disturbance, but may be also a fact of considerable importance in interpreting some disorder of nutrition. Further, such a condition as uric acid calculus may not always be dependent either on an increased excretion of uric acid, or even on the results of disturbed metabolism, but the formation of such a stone may be entirely due to some slight abnormality in the mode of the excretion of uric acid, owing to some alteration in the amount of saline ingredients in the urine. Anomalies in the excretion of certain urinary constituents may, therefore, be classified into one of two groups. The first where the results are dependent on some alteration in the mode of excretion, the second where the increased or diminished excretion is dependent on derangement of metabolism.

Although these various effects are well illustrated in the case of uric acid, there are other urinary constituents where the same series of phenomena can be seen, and, not the least important among these is the excretion of oxalic acid and the oxalates.

Oxalic acid, like uric acid, is excreted normally in small amounts, it being estimated that the daily excretion in a normal urine amounts to some twenty milligrammes of oxalic acid. Like uric acid, however, it is not excreted in the free form, but as a salt. Another resemblance to uric acid is to be found in the fact that the clinical importance of the excretion of oxalic acid lies rather in the form of its excretion than in the amount. Large quantities of uric acid may be excreted in the form of the soluble urates without giving rise to any trouble, whereas the

excretion of a small quantity of free uric acid may be followed not only by inconvenience but by serious complications. As mentioned before, the factors determining the mode of excretion of the uric acid include many beside the mere amount of the acid present; for instance, the degree of activity, the quantity of other salts present, the amount of pigment, etc. Similarly in the case of oxalic acid, this is excreted in the form of an oxalate which is kept in solution largely owing to the presence of acid phosphate of soda. The conditions determining the precipitation of oxalate of lime are not so well known as those determining that of uric acid; but, at any rate, it is certain that its deposition in crystalline form is not merely dependent on the amount present, although this, doubtless, is a factor. It is probable that in some instances the crystallization of oxalate of lime is determined by the presence of some material in the solution influencing the form of crystallization. Thus it is known that the presence of colloid material in the solution may cause the formation of large angular crystals, and it is further known that it is not uncommon for the nucleus of a urinary calculus to consist of a single abnormal large crystal. In such a case the formation of an oxalate of lime calculus may be in no way dependent on an anomaly in the amount or in the excretion of the oxalates present, but simply dependent on an anomalous form of crystallization brought about by the presence of mucus, blood, pus, or some other colloid material in the pelvis of the kidney. It is a matter of great importance to recognize that the formation of urinary calculi, whether uratic, oxalic, or phosphatic, may be entirely independent of any metabolic anomaly in the amount of these substances excreted.

There is, perhaps, unconsciously, too great a tendency to regard the presence of a stone as dependent on the excretion in increased amount of the particular substance composing the calculus, when it is in reality dependent on some disturbance in the balance of the other substances present in the urine. These considerations must not be pushed too far, as, no doubt, in isolated cases the formation of a calculus is dependent on the presence of the urinary constituent in question in largely increased amounts; but, as already insisted upon, this is not the sole cause, and in the opinion of many, not the most frequent cause of calculus formation.

Although the mode of the excretion of a particular urinary constituent is the more important factor in determining the formation of the calculus, the quantity of the substance present in the urine is the most important factor in affording evidence of the presence or absence of any disturbance of metabolism. Thus, the increased excretion of urates or phosphates may be of no importance from the point of view of the formation of a stone, but may be of great value in affording evidence of some disturbance of nutrition. The same is true in the case of the

oxalates. In all these conditions, however, it is most essential for the observer to be satisfied as to the existence of a real increased excretion, and not of mere alteration in the mode of the excretion. Thus the deposition of phosphates in urine is no real evidence of an existence of increased excretion, but merely of an altered relationship between the amount excreted in the form of soluble phosphates and the amount excreted in the form of phosphate of lime. Similarly the deposition of oxalate of lime crystals in the urine is no real evidence of the existence of what is sometimes loosely talked of as oxaluria. An increased excretion of oxalates can only be determined by quantitative estimation, and the habit of describing as a case of oxaluria one in which there is a more or less abundant deposition of oxalate of lime crystals is not to be recommended. The term oxaluria is not only used to describe the condition in which the urine contains an increased quantity of oxalates, but is also often applied to a group of symptoms mainly referable to the digestive organs, and an oxalic acid diathesis has been described much in the same way as a uric acid diathesis.

Uric acid is a substance that all observers are agreed upon has a double origin, being in part derived from the metabolism of the nitrogenous constituents of the food and in part from the nitrogenous metabolism of the tissues. In this respect it resembles urea, and it is impossible by diet to reduce the quantity of uric acid in the urine below a certain amount—in other words, below the quantity that is formed—owing to the metabolism of the proteid tissues of the body. It may, therefore, be justifiable to talk of a uric acid diathesis, since if the substance is formed by the metabolism of the tissue apart from the ingestion of food, it is at least conceivable that in disordered conditions the quantity formed from the tissues may be either increased or diminished.

In the case of oxalic acid, however, it is much more questionable whether such an expression as an oxalic acid diathesis is permissible, as it is by no means so clear that the oxalates of the urine have a double origin. There has been much discussion as to whether oxalic acid is formed by the metabolism of the tissues, and recent observers, such as Dunlop¹ and Baldwin,² have both come to the conclusion that oxalic acid is not formed by the metabolism of the tissues, although the latter qualifies the statement by saying that in health no oxalic acid or only a trace is formed in the body. If all the oxalic acid of the urine is derived from the food, an oxalic acid diathesis is really non-existent, and this matter is one of considerable practical importance.

¹ *Journal of Pathology and Bacteriology*, 1896, p. 389.

² *Journal of Experimental Medicine*, 1900, p. 27.

Dunlop concluded that oxalic acid is a constant constituent of the urine with the ordinary mixed diet, and such a diet always contains traces of oxalic acid or its salts. Dunlop considers that the daily excretion of oxalic acid varies, usually between ten and twenty-five milligrammes, the average being seventeen. Baldwin thinks the average quantity is usually normally below ten milligrammes, and that it may vary from a few milligrammes to as many as thirty. Both these observers, like others who have worked at the subject, emphasize the importance of not drawing any conclusion from the amount and number of the crystals of oxalate of lime present. As pointed out above, these afford no real indication of the quantity of oxalic acid present. This must be determined in all cases of accurate investigation by quantitative methods. Dunlop considered that the urine normally contains a sufficient quantity of calcium to precipitate the oxalic acid present, but that this precipitation is prevented by the acid phosphate of soda present, and that, therefore, its deposition in the urine in the form of crystals of calcium oxalate would often be dependent rather on variations in the urinary acidity, and thus on the amount of acid phosphate of sodium and other salts secreted, than on alterations in the amount of oxalic acid.

Although oxalic acid is not formed in the organism by the metabolism of the nitrogenous or carbohydrate tissues, there is evidence that it may result as a sequel of the fermentation of the contents of the stomach and alimentary canal. For this reason oxaluria should be looked upon rather as a urinary derangement consequent on gastric disorder, and not as a manifestation of a so-called diathesis. The treatment of the condition should, therefore, be directed to eliminating, as far as possible, oxalates from the diet, and also by measures directed to prevent undue fermentation of the gastric contents.

FUNCTIONAL ALBUMINURIA.

The question of functional albuminuria is always one of interest to the clinician, owing to the many difficulties that present themselves in the separation of this condition from organic renal disease. Many different types of functional albuminuria have been described by writers on the subject, and some have considered that these are but different phases of one and the same condition, others have rather looked upon them as quite distinct. Thus we have a dietetic albuminuria, a postural albuminuria, an albuminuria following bathing, especially sea-bathing, and a cyclical albuminuria. Among these the dietetic and the postural are those which have received the most attention. Another variety of so-called albuminuria that is seen from time to time is that

in which the albuminuria only appears in the urine after severe exercise, this, perhaps, has closer relationships with postural albuminuria than with any of the other varieties.

Mery and Touchard¹ record two cases of postural albuminuria, the so-called "albuminurie orthostatique" of the French, occurring in two children, aged respectively fourteen and a half and nine and a half years.

In the first of these, the girl, aged fourteen and a half years, there had been a prior attack of diphtheria, but the albuminuria that accompanies this subsequently disappeared. The child presented no physical signs of disease, the heart was normal, the liver was not enlarged, and there were no symptoms or signs of anæmia. The child never presented at any time any symptoms of renal disorder, such as any alteration in the quantity of urine or the presence of any cedema. The urine passed on first rising in the morning was invariably free from albumin, but that secreted during the day contained variable quantities. A large number of observations were made as regards the amounts of albumin present, which might reach as much as 8 grammes in the twenty-four hours, although this was very unusual; more usually the quantity amounted to but a few centigrammes, and, as the writers point out, it is very exceptional for the quantities of albumin secreted in this variety of functional albuminuria to exceed half a gramme in the twenty-four hours. The quantities of albumin secreted not only presented very great variations in their amounts, but it was apparently impossible to correlate these variations with any definite cause. Thus, for instance, on one day there was no albumin in the morning urine, that secreted in the evening contained $3\frac{1}{2}$ grammes, although during the day there had been no fatigue, and the evening meal had been an especially light one. If the patient was kept in bed all day the albuminuria entirely disappeared throughout the twenty-four hours, and this regardless of what diet the patient ingested, and, therefore, it was evident that the albuminuria was of the variety known as postural. Further investigation of the case brought out the fact that from time to time a sudden and great increase in the amount of albumin would occur, but it was impossible to determine what was the actual cause of these exacerbations in the albuminuria. The writers point out that the albumin disappears from the urine about forty minutes after the horizontal posture is assumed, and that it reappears as soon as the upright posture is resumed. Another remarkable and interesting fact is that there is apparently a maximum for the albuminuria appearing in a more or less regular fashion from eleven to twelve in the morning.

¹ Bull. d'Assoc. Med. des Hôp., 1901, No. 21.

The amount of the albumin would often diminish after this, notwithstanding the fact that the child was up and about and leading an ordinary life.

Speaking generally, the urine secreted in the evening before going to bed contained less albumin than that secreted toward the middle of the day, but there were exceptions to this. The writers think that perhaps for this reason the case should be classed as one of cyclical albuminuria, but, as they well say, is there really any great point of difference between cyclical albuminuria and postural albuminuria sufficient to make of one or the other a distinct variety? In both the albumin disappears when the patient rests in a horizontal position, and the writers very justly say that they do not consider that the time of day at which the albuminuria appears is a character of sufficient importance to found a clinical variety. It is certainly remarkable, if the albuminuria be dependent on the mere change of posture, that it should diminish in the course of the day, notwithstanding that the patient leads an ordinary life.

Another point of some interest that the writers record, is that in these cases of postural albuminuria the urine secreted during the night was always more abundant than that secreted during the day, and the density of the nocturnal urine was always considerably below that of the diurnal.

Perhaps the most important point alluded to by the writers in their communication is the fact that because an albuminuria has a postural character it by no means determines that the albuminuria is of functional origin. Several observers, especially Achard and Merklen, have shown that the albuminuria of Bright's disease and of other renal affections may sometimes present the characteristic of being greatly increased by the upright posture, and the writers record a case of a patient suffering from Bright's disease who had no albumin in the urine secreted during the night and only small quantities in the diurnal.

The writers think it is possible that too much importance has been ascribed to a clinical characteristic of many varieties of intermittent albuminuria. This postural characteristic, although of interest, is really not sufficient to be used as a basis of classification in order to separate a variety, more especially as this characteristic can be found in so-called cyclical albuminurias, and also in such pronounced and permanent forms of disease as some varieties of Bright's disease.

The writers further quote the case of a girl who had intermittent albuminuria, which at one time was present, both by day and by night, and subsequently only by day, and, as they very well say, in what group should such a case be classed? They conclude by stating that they look

on the group of postural albuminurias as one that is ill defined, and that the characteristic is in all probability a transitory one, so that the cases grouped under these headings very frequently have little or nothing in common. Merklen, in the discussion that followed this communication, quite agreed that in some cases of organic renal disease the albuminuria might present some of the features characteristic of postural albuminuria, but he considers that by far the greater number of cases of postural albuminuria are observed in children and young persons, and that they are dependent on functional derangement of the kidney, and he stated that he had never observed in any of these cases the subsequent development of any serious renal lesion.

At the same meeting, M. Achard and Loeper also record a case of postural albuminuria in a girl, aged eighteen years, whose younger sister, aged twelve, had a somewhat similar condition. In the case of the older patient the albuminuria disappeared almost completely by rest in bed. The upright posture and walking about for four hours will double the amount of albumin in the urine; diet, on the other hand, has no influence. Although the patient presents no obvious signs of renal disease, there are some symptoms pointing to the existence of a renal lesion—thus the general condition is poor, she is wasted, and suffers from frequent headache. In the case of the younger sister the albuminuria disappeared entirely in the horizontal position, in the elder it only underwent great diminution. The mother of these patients was also said to suffer from albuminuria. The writers thought that the older patient probably suffered from definite renal mischief, and they consider that both of them afford evidence of the difficulty of prognosis in some cases of postural albuminuria, and they also think that these cases show that it is impossible to separate as distinct affections a simple postural albuminuria, and a permanent albuminuria with postural exacerbations, inasmuch as these two conditions exist in two members of the same family. They draw attention to the fact that it has been shown that a postural albuminuria may be seen during convalescence from the albuminuria accompanying infective diseases, as for instance, diphtheria, and the same may be seen in some forms of scarlatinal nephritis. The authors think that the cases recorded by them show that a postural albuminuria may be an initial phenomenon in an albuminuria which may subsequently become permanent.

It would seem that many writers are agreed, therefore, that there is no such clinical entity as a postural albuminuria, but it is simply a characteristic that may be seen in a great variety of albuminurias of different degrees of severity, and both of so-called functional and of organic origin.

ALBUMOSURIA.

The interest excited by Bence Jones' observations on the occurrence of profuse albumosuria has been revived in recent years owing to the recording of several cases of a somewhat similar nature. Bence Jones recorded his case in the year 1847, and he noticed the characteristic reaction that the addition of nitric acid caused a precipitate, which disappeared on heating but reappeared on cooling. In his case the urine, as a rule, did not coagulate on boiling, but there were variations in this. Bence Jones not only described the fundamental reaction of nitric acid in this case of albumosuria, but he also noticed that the ribs were diseased and that at the post-mortem examination the ribs and the bodies of the vertebræ were quite soft, and, further, that the kidneys were healthy. Hamburger¹ records two more cases of Bence Jones' albumosuria associated with myeloma. In the first case the urine was pale, with a specific gravity of 1004, and on heating gave an abundant precipitate at a temperature of 55°. When boiled it became clearer, but it became more turbid on cooling. Acetic acid added to the fluid when the precipitate was marked caused it to disappear. Nitric acid gave a precipitate which disappeared completely on boiling, to reappear on cooling. The patient was a woman, aged forty-nine years, who had been quite well up to the present illness, and this began with sudden pain over the ninth left rib near its cartilaginous attachment. This pain disappeared in some three weeks, but subsequently a second attack of somewhat similar pain occurred in the eighth right rib. The patient presented no other signs of illness except that there was slight anæmia. The diagnosis of multiple myeloma in this case was based solely on the characteristics of the albumosuria, as the patient presented no physical signs directly implicating the bones. Some five months later, however, the patient developed a definite elevation over the ninth rib at the former seat of the pain, and, therefore, there is very considerable probability of the accuracy of the diagnosis.

In the second case the signs implicating the bones were more definite, and at the post-mortem examination myelomata were found in the skull, left scapula, both clavicles, the sternum, the right ilium, and the neck of the right femur. This patient had complained of a number of symptoms referable to her joints, stating that she suffered from rheumatism and a sprained hip, having had pain in the right groin and hip for more than a year. Six months before admission to the hospital she experienced a sense of lengthening of the left arm, and found that she was unable to use it, and a few days before admission the right leg gave

¹ Johns Hopkins Hospital Bulletin, February, 1901.

way, and she has been unable to walk since. The patient was markedly emaciated, and a number of tumors were found connected to the bones, one in the occipital region, one on each clavicle, another connected with the acromion process of the scapula, and another in the upper third of the right thigh. The case presented clinically the picture of multiple sarcomata of bone. The urine had a specific gravity, varying from 1012 to 1030, when heated, after acidification, to a temperature of 56° , a copious precipitate occurred, which dissolved in part on boiling and reappeared on cooling. The precipitate produced by nitric acid disappeared on boiling, reappeared on cooling, and the biuret reaction was marked. In other words, the patient presented all the characteristics familiar in cases of albumosuria.

It is remarkable that in the fifty years following Bence Jones' communication, according to Hamburger, only four observations of albumosuria associated with primary bone disease have been recorded, but within the last three years eight additional cases have been described, making thirteen in all. In eight of the thirteen cases tumors of the character of myelomata have been found post-mortem. In two other cases tumors were present during life, and in the remainder there was no record of a post-mortem. Hamburger in the above series excludes two cases of Bence Jones' albumosuria on the ground that in the one there was no evidence for presuming the existence of disease of the bones, while in the other, although changes existed in the bone marrow, it was not absolutely certain that they were identical with those associated with myeloma. The two cases excluded by Hamburger are first, one recorded by Fitz of myxœdema in which persistent albumosuria was a feature. There was no post-mortem in this case, and, therefore, there is a certain amount of doubt as to the existence of myeloma. The second case was one of lymphatic leukæmia, recorded by Askanazy; at the post-mortem examination changes were found in the marrow of the bones; this was of a thick gelatinous character and of the color of meat. Microscopically it consisted mainly of lymphoid cells, in addition to this there was a hyperplasia of all the lymphatic glands. Askanazy's case is certainly an apparent exception, as it would seem from the post-mortem to have been definitely a case of lymphatic leukæmia. Hamburger considers that, notwithstanding the difficulty in accurately determining the nature of a myeloma, there is considerable probability that Bence Jones' albumosuria is characteristic of myeloma. But it certainly is not an accompaniment of all cases of tumor of bone, and he quotes a remarkable case from Naunyn, who had observed a patient with multiple carcinomata in the bones, whose urine failed to give the Bence Jones reaction.

Usually the albumosuria is an early sign, and is persistent; occasion-

ally it does not appear until the illness is well advanced, and it may disappear before death. There are great individual variations in the amount of proteid present in the urine, in some cases it has amounted to no more than a $\frac{1}{4}$ or $\frac{1}{2}$ per cent., in others the urine has contained as much as $\frac{2}{10}$ per cent.

Hamburger concludes that there are no constant alterations in the urine apart from the presence of the albumose; the urine may, however, contain traces of albumin, and it may be abundant. In one case a milky urine was passed from time to time for as long as a year before the onset of any symptoms pointing to the existence of bone disease.¹

Hamburger considers in detail the characteristics of myelomata, and he points out that as a rule these tumors form masses of soft, reddish tissue, often ill-defined and replacing the normal marrow and osseous substance. The sternum, the ribs, the vertebræ, and the skull are more especially liable to be affected. The disease is most common in late life, and affects males more frequently than females, and its average duration is apparently some two years, but there are at least two cases recorded where the disease lasted, respectively, four and eight years. On histological examination, the structure of these tumors approximates to that of a round-celled sarcoma, though some writers have considered that the cell constituting the mass is really a plasma cell, and the tumor should be classified rather as plasmomata than as sarcomata. The growths are peculiar in the fact that, though they may affect the marrow of different bones, the tumors are only present in the bones, and no metastasis takes place in other tissues, so that in this respect they differ from ordinary malignant growths. It is for this, among other reasons, that instances of the disease are often described under other names: osteomalacia, malignant osteomyelitis, pseudoleukæmia, etc.

Hamburger considers that, speaking broadly, three types of the disease may be recognized clinically. In the first the essential features are paroxysms of pain referred to the bones. This is followed by considerable deformity and the development of cachexia, and associated with this is the albumosuria. As Hamburger points out, this is the group of cases that has been confounded with osteomalacia, but he does not consider that any true case of osteomalacia suffers from albumosuria, and so the differential diagnosis between the two conditions can be made. In the second group of cases tumors are present, frequently multiple, and accompanied by spontaneous fractures. Here the differential diagnosis has to be made from multiple metastatic deposits derived from a primary growth elsewhere. It is well known that multiple

¹ PROGRESSIVE MEDICINE, December, 1900, p. 229.

growths in bone are not very uncommon as a sequel to malignant disease of the mammary gland or of the thyroid body, and in both of these the primary growth may be overlooked. According to Hamburger, the presence of albumosuria determines this question, since this is not found in cases of metastatic deposits from a primary growth elsewhere, and in the second place in all cases where the albumosuria has been found the growth has turned out to be a myeloma. The third group of cases consists of those in which the bone symptoms are absent and the albumosuria is the only symptom. In some of these cases the patient has suffered from fever and sweats, and the case has resembled one of progressive anæmia, and such cases would not be recognized unless the significance of the albumosuria is correctly interpreted. Myelomata have been found in such cases post-mortem. Anæmia, fever, nausea, attacks of visceral pain, and the occurrence of palsy of the cranial nerves, as, for instance, the third division of the fifth, have all been described as exceptional symptoms in some cases of myeloma. It would certainly appear that the presence of Bence Jones' albumose in the urine would afford not only considerable suspicion of the existence of this malady, but that it is really characteristic of it.

URINARY CHANGES IN GASTRO-ENTERITIS.

Lesné and Merklen¹ consider, in a paper dealing with the gastro-enteritis of infants, the secondary effects produced by this malady on the liver and the kidneys. They have studied the renal changes, both pathologically and from the clinical side. Their paper also contains a summary of the results of former inquiries into the renal changes that are seen in the course of gastro-enteritis. Kjellberg was the first to notice a nephritis, and Pollak published two cases of thrombosis of the renal vein in the case of infants who had suffered from hæmaturia in the course of gastro-enteritis. Parrot considered that there were three common forms of renal lesions in such cases, thrombosis of the renal vein, uric acid infarcts, and so-called steatosis of the tubules. Parrot and Hutinel also observed, not uncommonly, thrombosis of the renal veins, which in two-thirds of the cases was bilateral. They considered that uric acid infarcts were very frequent during the first three months of life, but that they had no pathological significance. Where the renal veins were thrombosed the pyramidal portion of the kidney becomes intensely congested, and hemorrhage into the interstitial tissue to such an extent as to compress the tubules was by no means uncommon in the more serious forms. The cortical substance, according to Parrot,

¹ *Revue mensuelle des Maladies de l'Enfance*, February, 1901.

assumes the faded-leaf color, and the convoluted tubules frequently contained epithelial cells undergoing granular and fatty degeneration. In some cases the blocking of the renal veins only produced a cyanotic discoloration of the pyramids, the cortical substance remaining of the normal color. It is probable that these differences are referable to differences in the vigor of the circulation. Ebstein has recorded the occurrence, in cases of gastro-enteritis, of a so-called desquamative nephritis. Fischl and also Hutinel have both recorded, in cases of septicæmia arising from the gastro-intestinal lesions, changes in the epithelium of the convoluted tubules, and hemorrhages into the substance of the kidney, both beneath the capsule and in the glomeruli. In some instances miliary abscesses containing staphylococci have been found at the junction of the cortical and medullary substance. Bernhardt, in fifteen fatal cases of gastro-enteritis, found parenchymatous nephritis, and in many such cases he noticed that the epithelium of the tubules had undergone a fatty and granular degeneration. The tubules were obstructed with degenerated epithelium and casts, but the glomeruli were not profoundly affected. Other observers, more especially Simmons and Zamfiresco, have observed the same lesions. Lesné and Merklen state that their own observations have yielded more or less similar results. They describe that the kidneys present to the naked eye one of two forms: most frequently they are pale in color, but sometimes the organs are red and slightly enlarged. On section, the difference in the color of the cortical and medullary substance described by Parrot is most marked, and the capsule is often thickened in those cases where the course of the illness has been prolonged. Writers state that the most striking fact on microscopical examination is, that whatever has been the course of the illness, congestion is the most marked lesion in the kidney. In the more acute forms the congestion is wide-spread, in the less severe forms it is more localized, but it is always well marked in all cases of gastro-enteritis which have presented pulmonary complications. The capillaries of the pyramids are intensely congested, and it would seem occasionally as if there had been intertubular hemorrhage in the cortical substance, and the distended capillaries compressed the convoluted tubules. Bowman's capsule is filled by the distended glomerular tufts, and the epithelium of the glomerulus often shows signs of proliferation, and sometimes hemorrhages are present in the capsule. In some instances localized collections of leucocytes are found scattered through the cortical substance and separating the convoluted tubules or surrounding the capsule of Bowman. The tubular changes are almost entirely restricted to the convoluted tubules, and the authors have occasionally observed that the cells present a typical example of coagulation necrosis. In the less acute forms of gastro-enteritis all stages are

found between granular degeneration of the epithelium, more or less extensive in its distribution, and complete shedding of the epithelium of certain tubules. The authors conclude that the lesions of the kidneys in gastro-enteritis have really not got any specific characters, but are quite comparable to those seen in adults as the result of acute infections. So that, according to the length of the malady, congestion only may be seen, or congestion followed by epithelial changes, or a commencement of fibrous overgrowth.

From the clinical stand-point albuminuria has been observed by many authors, but in addition to that, two other symptoms are considered to be of renal origin, namely, dyspnoea and the presence of oedema; and Lesné and Merklen state that they have observed dyspnoea in many cases clinically where the autopsy afforded no obvious explanation for it, and they consider that very likely it is of renal origin. Oedema of the anterior surface of the legs and of the dorsal surface of the feet has often been noticed, but a general oedema, such as is seen in Bright's disease, is exceptional. There are other symptoms which the writers consider of less significance, such as periods of drowsiness, alternating with agitation and restlessness. Convulsions also, which are so common in children, can scarcely be looked upon as of uræmic origin, and the same remark applies to the presence of a subnormal temperature. The authors do not agree with Koplik that any particular variety of vomiting can be associated with the renal changes, and they think that it is more reasonable to suppose that the vomiting is entirely of gastric origin. In a few instances, contraction of the pupil, such as that seen in uræmia, has been observed. The authors consider that the presence of oedema, dyspnoea, and occasionally contraction of the pupil, are the most reliable clinical symptoms pointing to the probable existence of renal changes.

In discussing the changes in the urine associated with the gastro-enteritis of infants it is very essential, first of all, to be acquainted with the normal composition of the urine in infants. The authors state that up to the tenth day of life infants do not secrete more than 80 to 100 grammes of urine in twenty-four hours, and that after that the quantity increases to 250 to 300. Subsequently to the fourth month of life as much as 500 grammes may be excreted per diem. The urine is clear, pale, very acid, and the specific gravity varies from 1002 to 1005 during the first month. Occasionally it rises as high as 1007 by the tenth week. The toxicity of the urine is also less than that seen in adults. The urea excretion of infants is, approximately, from 0.3 to 0.5 grammes of urea per kilogramme of body-weight in the twenty-four hours; the chlorides are present in scanty proportion. According to the authors, urobilin is not present in the urine of newborn children and of infants,

and indican is also absent. The authors consider that neither albumin nor sugar is present in the urine of infants in the normal condition, although albuminuria is really very frequent, but they look upon it as pathological. The so-called glycosuria of infants is probably related to the presence of uric acid and creatinin in the urine, and is not a true glycosuria. In gastro-enteritis the urine presents very considerable changes. If the gastro-enteritis is mild and unaccompanied by high fever, the urinary changes are very slight. But if the gastro-enteritis is more severe, very considerable urinary changes are observed. Thus, the quantity may fall from 200 grammes to 50 or 30 grammes in the twenty-four hours. The urines are dark in color, turbid, and the acidity is increased. Such urines, however, according to the authors, are extremely prone to decompose with even greater rapidity than in health. The specific gravity may rise to 1015 or 1020. If such urines are examined cryoscopically, it is found that these concentrated specimens are hypertonic. Biliary pigments are not usually found in the urine. In thirty-three out of forty-six cases examined the urine contained indican. The excretion of urea necessarily undergoes progressive diminution in the course of gastro-enteritis, and the quantity excreted may fall to less than one-half the normal proportion excreted in health. This diminution is necessarily largely dependent on the vomiting and diarrhoea, and is not to be regarded as an indication of any functional disturbance of the liver. The toxicity of the urine is also considerably increased, and the authors describe that after the subcutaneous injection of the sterilized filtered urines secreted during gastro-enteritis into rabbits, the latter died in from sixteen to twenty-five days, and within the first few days following the injection the urine secreted is albuminous. Albuminuria is generally present, and in the more severe forms of gastro-enteritis the albumin appears early, and persists until death. In the slighter cases the albuminuria is liable to appear later, and the authors state that in all cases of recovery from gastro-enteritis the albuminuria disappeared after convalescence. Granular casts, leucocytes, and a few blood corpuscles are also found present in the urine. Methylene blue is usually excreted by the kidney in a more or less normal fashion, and only two out of seven cases showed any notable diminution in the rate of its excretion. The authors consider that the most constant renal symptoms are the presence of albuminuria accompanied by granular casts. They do not consider that the prognostic indications afforded by examination of the urine are of any very great importance, although the secretion of dense, hypertonic albuminous urines shows that the kidney structures are affected, and, to a certain extent, increase the gravity of the prognosis.

URINARY CHANGES IN SYPHILIS.

The renal changes associated directly or indirectly with syphilis are numerous and varied. The syphilitic nature of several affections of the kidney is apparently not always recognized, although such affections as amyloid degeneration and the presence of gummata in the kidney in tertiary syphilis are well known. The relationship of nephritis in its many different forms to syphilis is by no means so well recognized, and yet nephritis in varying degrees of severity is not a very uncommon complication of secondary syphilis, and especially, perhaps, during the first year following syphilitic infection. This nephritis, as pointed out in *PROGRESSIVE MEDICINE*, in December, 1900, p. 256, may, according to Delamare, be either acute or subacute, the chronic form being rare.

The acute nephritis complicating secondary syphilis is sometimes a very serious affection, and may even be fatal; and it is remarkable that in some cases albuminuria is the most marked symptom, the other phenomena of renal disease, such as dropsy, being absent. The albuminuria may be extremely abundant, the urine being solid with albumin, and such cases may become complicated with and fatal from uræmia.

Syphilis may apparently not only directly produce nephritis of varying degrees of severity, but it may also act as a predisposing cause to the development of this complication.

Patoir¹ deals in his memoir rather with the question of the disturbance of the urinary functions in cases of syphilis than with the actual production of these complications, but his paper is of considerable value and interest in drawing attention to the very large proportion of cases in which the renal functions are more or less seriously interfered with in cases of syphilis.

Patoir draws attention to the fact that, although it has been known for many years that syphilis may give rise to such specific lesions as gummata in the kidney, it has really also been known that inflammatory and degenerative lesions, in fact nephritis of all kinds, acute or chronic, severe or slight, may also be the sequel of syphilitic infection. Further, that the routine examination of the urine has shown in a very large proportion of cases that without any other sign of nephritis, albuminuria was often seen at the moment of outbreak of secondary symptoms. This albuminuria resembles, in many respects, that seen in infective diseases.

Patoir dealt largely with the question as to whether there was any evidence to show that even in the absence of albuminuria the functions

¹ *Archives Générales de Médecine*, Avril, 1901, p. 385.

of the kidney were impaired during the course of syphilis. In order to examine this question fully the author relied mainly on a chemical analysis of the urine and on investigation bearing on its toxicity.

In addition to this, observations on the permeability of the kidney were carried out by means of the methylene-blue test, and also by the method of cryoscopy. The author points out that the former two methods are of more service than the latter. In investigating the chemical composition of the urine, especial attention was paid to the quantity, the specific gravity, the reaction, and especially to the quantity of urea, of chlorides, of phosphates, of uric acid, and of total nitrogen. In this way a very complete and systematic analysis of the fluid was made. The urinary toxicity was measured in the usual way by the injection of quantities of filtered urine into the circulation of rabbits. Methylene blue was injected in quantities of 5 centigrammes and the urine collected a quarter of an hour after the injection, then half an hour, one hour and two hours after, up to the twelfth hour. After the twelfth hour the urine was only examined every six hours. The injection of methylene blue, of course, gives accurate information as regards the permeability of the kidney to this substance, but, as has been pointed out by several observers, and more especially by Lépine, quoted by Patoir, there is nothing to show that deductions drawn from the behavior of the kidney to methylene blue can be applied also to its permeability in relation to the normal constituents of the urine. In a general way the rate of elimination of methylene blue is much the same as that of the normal constituents of the urine. One of the main uses of this method is that it serves as a control to other methods having for their object the investigation of the efficiency of the renal filter. Patoir considers, when the methylene-blue test shows the kidney to be as permeable as normal, that any alterations in the composition of the urine should be considered as dependent rather on an alteration of metabolism than on renal changes, whereas, if the permeability of the kidney is shown to be abnormal it is probable that the state of the kidney has an influence on the disturbance of the renal functions. Patoir very truly observes that observations on the toxicity of the urine are not of a character to allow themselves to be expressed in mathematical terms, and that the results depend upon many complex characters. He also considers that the cryoscopic method has not yet been sufficiently tested for its clinical and practical value to be accurately known. The author, therefore, lays most stress for these reasons on the chemical investigations.

Forty cases of syphilis have been examined, the majority of them being from seventeen to thirty years of age. They were carefully selected as not having suffered from other acute specifics. In the major-

ity of cases the syphilis had not been treated, and inasmuch as they were mainly hospital patients the diet was much the same for all of them. In a third of the cases the quantity of the urine and specific gravity were higher than normal, the principal abnormal substances found were albumin, sugar, and urobilin. Albumin was present in six cases out of the forty, but in only two cases was there a sufficient amount to determine the quantity present, which was never more than $\frac{1}{2}$ a gramme per litre. In all the other cases the albumin was only present in traces. In the two cases where the albumin was more abundant the syphilis was severe, and one of them suffered from pleurisy. In two out of the other four cases the patients were elderly. Sugar was only found on one occasion; the quantity amounted to $2\frac{1}{2}$ grammes per litre.

As regards the normal constituents of the urine, chemical analysis showed that the urea was usually abundant, and in twelve out of the forty cases was excreted in greater quantities than those usually seen in health. In nine cases the quantities excreted were a little below those usually seen in health. The author considers that from 0.35 to 0.43 grammes of urea per kilogramme of body-weight represents the normal limits of health. The increased urea secreted was seen in the younger patients. The author considers that the increased secretion of urea is dependent on a disturbance of nutrition, and may be an indication of the reaction of the organism against the syphilitic infection.

The chlorides are usually fairly abundant in the urines that are rich in urea, and the same remark applies to the phosphates, but less so in the case of uric acid, as it is not very uncommon for this substance to be present in increased amount when the urea is diminished. Patoir found that the toxicity of the urine was in the great majority of instances less than normal, and this result has also been confirmed by Soual.¹ In one case a rabbit received as much as 200 c.c. of urine, and survived for six weeks without manifesting any symptoms. The author is not prepared with any explanation on the somewhat remarkable fact of the diminished toxicity of the syphilitic urines.

In nineteen out of the forty-cases methylene blue was eliminated by the urine in a normal fashion. In twelve cases the rate of elimination was somewhat above the normal. In seven cases the elimination was less than normal.

Patoir summarizes his conclusions that in approximately half the cases of syphilis the urinary functions are affected during any active stage of the syphilitic infection; that is to say, either at the moment of the outbreak of the secondary symptoms or at a later recrudescence.

¹ Thèse de Toulouse, 1900.

It is at this time that abnormal substances, like albumin, urobilin, and sugar, appear in the urine, and it is also then that the quantity and density of the fluid are altered. The effects produced, however, are not the same in all the cases. In young persons where the kidney is healthy, he considers that the urinary excretion tends to become more active, and that the quantity and density of the urine increases, and that the elimination of even such a substance as methylene blue is increased. When the patients are older, and there are reasons to think that the kidney already is not as permeable as formerly, he considers that a syphilitic outbreak is liable to diminish the quantity and increase the density of the urine, to diminish the excretion of urea and to somewhat impair the elimination of methylene blue. In tertiary syphilis the urinary functions are apparently not affected, unless, of course, the disease directly involves the kidneys. In all cases of syphilis the toxicity of the urine is diminished considerably at the moment of the outbreak of syphilitic manifestations.

Patoir considers that syphilis in half the cases at the time of the outbreak of cutaneous eruptions disturbs the general nutrition of the body. He thinks that in young subjects it causes an increased activity of nutrition, probably as a means of defence of the organism ; in more elderly persons this disturbance in nutrition does not occur. In a large number of cases, and especially in mild syphilis, there are no effects in connection with the urine tending to show that the functional activities of the organs of the body have been seriously compromised by the disease.

BRIGHT'S DISEASE IN THE YOUNG.

Bright's disease and all forms of nephritis are maladies especially affecting adults ; but, notwithstanding this, they occur, perhaps, with rather more frequency in the young than is usually thought. This is not only true of nephritis in its ordinary acute and subacute forms, but is also the case with the more chronic manifestations of these maladies. This fact is one that is necessary to bear in mind, inasmuch as there can be but little question that chronic nephritis is very frequently chronic from the outset rather than necessarily the sequel of a former attack of acute nephritis. The most chronic and insidious forms of chronic nephritis also occur in the young, and even such an affection as the so-called granular kidney is by no means such a rarity in the young as is sometimes thought. The more chronic forms of Bright's disease, especially those associated with contracted kidney, and the granular kidney, are affections so insidious that they are extremely liable to be overlooked in adults until the disease has advanced to such an extent as to produce sudden and alarming symptoms. They are still more

likely to be overlooked in children, owing to the general impression existing that such maladies are so rare in childhood.

It is often difficult, from the records of writers on the subject, to determine exactly what form of chronic nephritis is present in the young, inasmuch as so many writers use the term "granular kidney" as inclusive of almost all forms of chronic renal disease in which the surface of the organ is granular. Other writers restrict the term to what many have been described as the small red granular or raspberry kidney, which is usually accompanied by pronounced arterial changes and considerable cardiac hypertrophy, the other form of atrophied kidney being described as an atrophic form of Bright's disease, or as a contracted white kidney or small white kidney. The nomenclature of all these diseases is at the present time in rather a confused state, but we must recognize that the distinction between the various forms are not only anatomical, but are also clinical, and perhaps in many instances also etiological. There is one form of chronic renal disease which occurs both in children and adults, in which the organ is small, granular, but usually pale in color; the capsule, although thickened, is not very adherent, and on stripping leaves a surface on which the granulations are extremely well marked and prominent. In such cases the arterial system presents changes of a moderate degree of severity, and the heart is also usually hypertrophied. The degree of cardiac hypertrophy, however, and even its presence, cannot be correlated with the degree of atrophy of the renal substance. Some cases are seen, even in the young, where the renal changes have advanced to a high degree, and where there is little, if any, cardiac enlargement. The ordinary type of such cases, where the cardiac hypertrophy and arterial changes are marked, form a very definite clinical picture, characterized by the secretion of a highly albuminous and moderately abundant urine, the absence of dropsy, with death usually resulting from uræmic complications. In many of these cases, especially in adults, no history of a previous attack of acute nephritis can be obtained, and in some such cases no history, even of the attack of an acute specific fever. It is possible that in some cases this condition results from a prior attack of acute nephritis. Many writers speak of this form of renal disease as granular kidney, and consider that the considerable albuminuria and the epithelial changes present in the kidney are dependent on a superimposed catarrhal and more or less acute nephritis. However this may be, the type sketched above is, in the opinion of the writer, a definite clinical entity, and may occur in the quite young as well as in young adults.

In the other, or true granular kidney, the organ is usually red, the capsule extremely adherent, tearing the renal substance on stripping, and arterial changes and cardiac hypertrophy are extremely well

marked. Such patients secrete during life, as is well known, a pale, dilute urine containing a small quantity of albumin, or even at times none. Drs. Brill and Libman¹ record a case of chronic interstitial nephritis in a girl of fourteen, and have brought together the main facts known with reference to the occurrence of this malady in the young. These writers quote Hübner's statistics, where, out of 251 cases of chronic nephritis, 37 occurred in children. Hübner altogether saw 65 cases in children, but of these only 4 were instances of what is spoken of as contracted kidney. Bartels, out of 33 cases of so-called chronic interstitial nephritis, found but one in a person under twenty, and aged eighteen years, and Dickinson has recorded one in a patient under twenty years, out of a total of 308 cases. Of Hübner's four cases, three occurred in males, nine, fourteen, and twenty-four years of age, and one in a female aged eleven years. Writers quote that, according to Hübner, there are only records of seven such cases that can be looked upon as primary contracted kidneys, owing to the absence of any history of prior acute attack. The ages of the patients at the time of death varied from five to fourteen years. In some cases recorded, even in children of six and twelve years of age, in addition to the renal lesion the arteries were thickened. Drs. Brill and Libman have, however, succeeded in collecting some other instances, as for instance, one recorded by Baginsky, in a girl aged four years, and two others by Ashby and Wright, in girls aged ten to eleven years. Their own case occurred in a girl of fourteen, who gave no history of a previous acute illness, but she had suffered a year prior to her death from œdema of the face and feet. Her health, however, had never been very robust, the child being weak and undersized. The patient presented signs of marked arterial changes, together with considerable cardiac hypertrophy, and she died with pericarditis. The clinical course of the disease in this case was remarkable, owing to the occurrence of hemorrhages in a large number of situations. Hemorrhage from the gums, hemorrhage into the lung and spleen, cerebral hemorrhage, and hemorrhage into the mesentery are all described. The right kidney weighed 59 grammes, and the left 34½ grammes. The cortex was greatly diminished in width, and the microscopical examination showed the presence of a "marked chronic interstitial nephritis." The authors point out the difficulty that often presents itself in the diagnosis of such cases in determining whether the lesions are primarily cardiac and secondarily renal, or primarily renal and secondarily cardiac; and they lay stress on the importance of the examination of the heart, and especially the

¹ Chronic Interstitial Nephritis in the Young; *Journal of Experimental Medicine*, vol. iv., Nos. 5 and 6.

arteries. The existence of high tension shown by the accentuation of the aortic second sound, together with the pulse characters and the thickening of the arteries, afforded evidence in their case that the disease was not primarily cardiac. The arterial changes in this case were very advanced, and the authors discuss the question as to whether they were secondary to the renal lesion or not. They state that the lesions were quite as marked as those seen in well-marked cases of arterio-sclerosis in adults. The family history of the author's case was interesting, in the fact that three out of the six surviving children showed a tendency to the development of chronic interstitial nephritis. Six children had died in infancy from unknown causes; of the survivors, three showed no abnormality in health or in the condition of the urine. In one the urine was of low specific gravity, 1016, contained no albumin, and the heart and arteries were normal. In another, aged nineteen years, there was marked anæmia. The pulse was of high tension, the urine of specific gravity, 1001½, contained albumin, and the heart showed signs of hypertrophy. In another, aged twenty-four years, there was some anæmia, the heart was hypertrophied, the arteries thickened, the urine was of specific gravity of 1012, but it did not contain any albumin in the one examination that was made. The writers draw attention to the occurrence of renal disease in several members of one family, and allude to Dickinson's well-known case, in which two members of the first generation had albuminuria, two members of the second generation also had albuminuria, and out of the six children in the third generation five had albuminuria. They also quote a record of Eichorst, in which the grandmother died of uræmia, the mother and a daughter both suffered from chronic interstitial nephritis, and two sons died of uræmia.

The writer knows of an instance in which, although the parents were healthy, the only daughter died of uræmia at the age of fourteen years, and the only son presented marked physical signs of chronic nephritis at the age of nine years.

The records of all these cases, and of others that might be adduced, show that the malady is not so uncommon as at first sight might appear, and also the extreme importance of examining the urine and being on the lookout for the existence of chronic renal disease in the young, owing to the ease with which the malady may be overlooked from its insidious nature. Drs. Brill and Libman draw attention to the well-known fact that it may be confused with diabetes insipidus, and in other instances that it may really be the cause for a long-continued and obscure anæmia. This is a fact which is not only of importance in childhood, but also in the investigation of the anæmia of adolescence, as it is by no means uncommon for patients with advanced and serious renal disease to come under observation as apparently cases of chlorosis.

Some years ago the writer¹ recorded a series of six rapidly fatal cases of contracted kidney occurring in young women where the patients came under observation on account either of chlorotic symptoms, or else of very vague symptoms of ill health that in no way suggested renal disease, and still less serious renal disease. In such cases the examination of the urine is of fundamental importance, but the nature of the malady can often be detected by ophthalmoscopic examination, owing to the presence of albuminuric retinitis, and the routine examination of the fundus in all cases of headache and of anæmia will lead to the recognition of many of these cases of obscure renal disease.

THE NEPHRITIS OF PREGNANCY.

Nephritis and Bright's disease are not only dependent on a great variety of different causes, but they also exist in a considerable number of different forms. One of the most difficult problems in the pathology of these affections is to determine whether one and the same cause will give rise to the variety of different forms of the disease. Another problem that presents itself is the question whether a single toxic substance such as lead, or the toxin of a disease, is capable not only of giving rise to a number of different forms of nephritis, but whether these are merely stages in the action of the toxic body.

It is possible, for instance, that the form of Bright's disease known as the contracted white kidney, or one of the varieties of the so-called granular kidney, may be produced by the action of such a poison as lead. The further question may then present itself whether this contracted form of Bright's disease is the sequel of a previous parenchymatous nephritis, or whether it has evolved steadily and continuously in the same form as that in which it is ultimately fatal. It was a favorite doctrine at one time that a toxic substance might produce acute nephritis, which would then in the course of time become a chronic parenchymatous nephritis, and this, in time, owing to the overgrowth of fibrous tissue, etc., might become a granular or contracted kidney. This view was far more commonly held a few years ago than it is at the present time, owing to the fact that it is so frequent for cases of chronic nephritis in all its forms, interstitial and parenchymatous, to occur without any previous history pointing to the former occurrence of acute nephritis. Although in many cases it is certain that the chronic forms of the disease originate as such and are not the sequel of acute nephritis, yet in other cases it would seem as if a contracted kidney might be the sequel of various other forms of nephritis. The problem

¹ Practitioner, 1898.

is difficult enough in the case of the action of such a definite toxic substance as lead, which may undoubtedly produce, on the one hand, a true granular kidney, and on the other hand, certain forms of chronic Bright's disease, and more especially the contracted white or atrophic kidney. The difficulties are far greater in the case of nephritis which is brought about by the action of the toxins produced in disease.

The nephritis complicating pregnancy must be included among those forms of Bright's disease and nephritis which are produced, in all probability, by the action of toxins, although in this instance the identity of the toxic body or bodies is unknown.

Gaucher and Sergent¹ deal especially with the more serious forms of nephritis arising in pregnancy, and they record five cases where the malady not only became chronic and was fatal, but where the main lesions were in the interstitial fibrous tissue of the organ. They draw attention to the very large number of conditions that may give rise to albuminuria and lesions of the kidney during pregnancy and parturition, and they eliminate from consideration all conditions consecutive to the compression of the ureters by the gravid uterus, and also all lesions of the kidney which are in any way dependent on puerperal septic infections where the relationship with the pregnancy is really an indirect one. When these are eliminated there still remain a considerable number of varieties of albuminuria associated with pregnancy. Many forms of albuminuria associated with pregnancy are not apparently dependent on the presence of nephritis, or, at any rate, of a nephritis that is in any way serious. At the same time these authors consider that all forms of albuminuria associated with pregnancy must be looked upon with suspicion as tending to show that the kidneys are not quite sound, or, as they say, that if auto-intoxication is sufficient to produce an albuminuria, is it not possible that in course of time the kidney may become damaged? They consider that it is almost impossible to draw a hard-and-fast line between a transitory albuminuria associated with pregnancy and dependent, perhaps, upon a blood dyscrasia on the one hand, and chronic Bright's disease, produced by pregnancy, on the other hand. Great as is the difference between these two extremes, they are connected by a series of cases of varying degree of severity of transitory nephritis, acute nephritis, and subacute nephritis. Further, it would seem that the albuminuria of pregnancy, even if dependent on an organic lesion, may disappear entirely, but much more often there remains a permanent lesion or weakness of the kidney which, at any rate, reveals its existence at the next pregnancy. As Gaucher and Sergent point out, there are many cases in which albuminuria is the

¹ Rev. de Méd., January, 1901, No. 1.

only symptom which is observed, and this even may be temporary and vary from time to time during the course of the pregnancy. Such an albuminuria will often disappear after confinement, and, unless other symptoms are produced, the lesion of the kidney must be regarded as slight. It is remarkable that in some cases of this kind, where no other symptoms are produced except the presence of albuminuria, how the latter does not clear up until some time after delivery. Pregnancy is not, however, the only condition in which albuminuria is the sole symptom pointing to the existence of serious renal disease. Cases of nephritis in the experience of the writer are sometimes seen where the urine is loaded with albumin without the presence of any other symptoms, such as dropsy, or hæmaturia, pointing to the existence of renal disease, but yet where uræmic symptoms may develop, and even cause death. In these severe forms of albuminuria, casts containing renal elements are, however, always present. Gaucher and Sergent point out that in some cases of albuminuria of pregnancy the presence of other symptoms, such as slight fever, transitory œdema, and the diminution in the quantity of urine, point to the conclusion that definite nephritis is present, and they consider that this form of the malady is especially apt to attack primiparæ and to occur during the later periods of pregnancy. They consider that such a form as this may become completely cured after delivery, but that on the other hand it may be the beginning of a permanent lesion and become chronic. It is more usual, however, for the transition from the albuminuria of pregnancy to chronic renal disease to take place after a period of improvement of variable duration during which the albuminuria may not only diminish in amount but may even disappear. Gaucher and Sergent consider that when the albuminuria of pregnancy becomes chronic the typical symptoms dependent on the production of interstitial nephritis occur, the most important of these being the well-known *bruit de galop*. These authors consider that, generally speaking, it is possible to distinguish two periods in the evolution of this nephritis when it is becoming chronic. In the first the characteristic features are the existence of œdema and the secretion of a scanty urine containing a large quantity of albumin and abundant casts, and they think the duration of this period, although variable, does not usually last more than a few months. If no improvement takes place the kidney lesion becomes definitely chronic, the *bruit de galop* becomes developed, and the urine assumes the characters of that seen in the granular kidney. In many cases the transition between these two forms cannot be so readily observed, owing to the fact that the progress of the case is not uniform, but is interrupted by periods of remission, with more or less complete subsidence of symptoms. This, however, is also not a peculiarity of the renal disease of pregnancy, but

is seen in most, if not in all forms of chronic Bright's disease, the progress of the case not being necessarily a steady one from bad to worse, but being often interrupted by periods of great amelioration. Gaucher and Sargent lay particular stress on the occurrence of interstitial nephritis or granular kidney as a result of pregnancy, and they also lay great stress on the presence of the *bruit de galop* as clinical evidence of the occurrence of this development.

In considering the question of the anatomical changes that are seen in such cases, these writers recognize two forms of interstitial nephritis, one, that which is ordinarily spoken of as the red granular kidney associated with arterial changes, and, perhaps, of arterial origin, and which, as they say, might be called primary interstitial nephritis, and a second variety of so-called secondary interstitial nephritis, which is a sequel of lesions of the epithelial structures of the kidney. The best instance of the second form of the disease is, perhaps, afforded by the kidney lesion seen as a result of the action of lead. These authors consider that such a kidney is essentially an example of mixed nephritis, where, notwithstanding the epithelial lesions, or, rather, notwithstanding that the epithelial lesions were the earliest produced, the interstitial fibrous lesions ultimately predominate and the overgrowth of fibrous tissue is very considerable. Gaucher and Leger both point out that, notwithstanding the great overgrowth of fibrous tissue, the kidneys are not always necessarily small, although, in some instances, they are greatly deformed and atrophied. In others, however, they are large and white, but their consistency is always increased, and the capsule is always unduly adherent. The heart is hypertrophied, and frequently to a very considerable extent.

The main result of their paper is to adduce anatomical and clinical evidence that pregnancy, apart from other causes, may apparently produce forms of renal disease indistinguishable from those produced by the action of such a definite mineral poison as lead. They conclude by saying that they consider that the chronic nephritis of pregnancy resembles, from the etiological, anatomical, and clinical stand-points, the nephritis that is produced by slow intoxication, and, more especially, those seen by the action of metallic poisons. One of their most important facts is that whatever the actual cause of the mischief originally, it is capable, once being started, of progressing.

In the less serious cases the lesions of the kidney are apparently less marked, and, according to these writers, probably confined to the epithelial and glomerular structures, and in such instances, when the cause which has produced them ceases to operate, the kidney soon recovers its normal functions. In the second class of cases the action of the toxic body on the kidney is more severe, and the lesion, instead of remaining

limited to the epithelial structures, affects also the interstitial fibrous tissue. This effect may apparently be produced either by the more prolonged action of the toxic substance, or else by its repeated action.

Gaucher and Sergent consider that all toxic forms of nephritis tend to have the same course, whether the toxic substance is a mineral poison, or is of vegetable or of animal origin.

VARIETIES OF URÆMIA.

Although the toxic condition known as uræmia resembles in some respects other toxic states produced in disease, such as diabetic coma and the coma seen in grave hepatic diseases, yet there is one great point of difference. In acetonæmia and in cholæmia there is no very great variety in the clinical symptoms in different cases, whereas in uræmia there are a great number of clinical varieties. This applies not only to such a fundamental division as that into the acute, the subacute, and chronic uræmia, but also as regards the varieties included under each of these headings. In some cases the main disturbance is one affecting the highest cortical centres and producing a condition closely resembling that of mania. In others the effect, although still an excitant one, is produced on lower centres, producing in one case epileptiform seizures, in another cramps and twitchings. In other instances the main effect produced is coma, in others restlessness and great dyspnœa. In uræmia, therefore, there is not only great variety as to what part of the central nervous system is affected by the poison, but, further, there is the remarkable fact that, in some instances, the toxic effect is an excitant one, causing convulsions, delirium, mania; in others a depressing one, causing paralysis or coma. Although frequently the depressing effect is seen as a more or less terminal phenomenon after a preliminary excitation, this is by no means invariable, and a pure depressing or a pure stimulant effect may be seen. The most common depressing effect is, undoubtedly, the production of coma, but, as is well known, it is not very uncommon for other phenomena of an allied character, as, for instance, dimness of vision, and even sudden and complete amaurosis, to be produced. This abolition of the function of nerve centres is seen not only as regards the higher centres of the cortex and the sensory centres, such as those of vision, but more exceptionally the same phenomena are seen involving the motor centres and producing various forms of palsy. The production of palsy in renal disease may be dependent on many different causes, more especially upon vascular lesions associated with the high tension and the arterial degeneration which so frequently accompany renal disease; for this reason there is often considerable

doubt in the diagnosis of a sudden palsy in a patient suffering from chronic renal disease, and there is always a tendency to look upon the lesion as of vascular origin rather than of toxic or uræmic origin. Brodier¹ records two cases of hemiplegia where no gross lesions were found post-mortem, and which are, probably, to be looked upon as cases of uræmic hemiplegia. He draws attention to the point mentioned above of the difficulty of diagnosing these conditions clinically.

In many cases the hemiplegia dependent on uræmia is of sudden onset, and occurs only during the terminal stages of the malady, but in Brodier's cases the record is somewhat different. His first patient, a woman, aged forty-five years, had not suffered any previous illness, but for the last two years had suffered from dyspnœa, palpitation, and cardiac oppression, together with headache. Eighteen months before admission she had experienced numbness and tingling in the left upper extremity. After this had persisted for about fifteen months she found that the arm was weak, and a few days afterward the leg of the same side became weak, and two days after the involvement of the leg the left side of the face became involved. On admission the patient presented an incomplete left hemiplegia of a flaccid type. There was no loss of sensation, the knee-jerks were not exaggerated, and the plantar reflex was flexor in type. Cardiac hypertrophy was present, and there was some increase in the pulse tension. There was no œdema, the urine was pale, and, although it contained no albumin on the day of admission, subsequently it did in moderate quantities. The case was diagnosed as suffering from Bright's disease and the effects of an old cerebral hemorrhage. She was treated on a rigid milk diet, and her general symptoms underwent an improvement, but none was observed in the hemiplegia. The date of the first admission was October, 1899; she was readmitted in June, 1900, when the hemiplegia was still present, still flaccid and incomplete, and she was again placed on a rigid diet. On June 18th she began to suffer from delirium, and at this period slight œdema was present. The delirium increased, and death occurred on June 26th, in a state of coma, convulsions never having been present. At the post-mortem the heart was found hypertrophied, the kidneys were small, the capsule adherent, and the cortex diminished in thickness. The cerebral vessels were very slightly atheromatous, but the brain presented no lesion, and the meninges were normal.

The second case, also a woman, aged fifty-six years, was admitted in April, 1900. She had never suffered from any serious illness, but four years previously she had her first attack of right hemiplegia, which

¹ Arch. Gén. de Méd., October, 1900.

only lasted a few days. A year later a second attack of right hemiplegia, accompanied by aphasia, occurred suddenly. In neither case was there any loss of consciousness, and both attacks were apparently incomplete ones. Since the second attack the limbs on the right side have remained rather weaker than those on the opposite side, and she has experienced some difficulty in talking. A year ago a third attack occurred, accompanied by loss of consciousness, which lasted two hours. Speech was rather more affected, and the weakness of the limbs on the right side was increased. But after a few days the condition returned to that which it was prior to the third attack. For the last five or six years the patient has complained of fatigue, and during the last two years the body has undergone some wasting. Two months prior to admission œdema of the legs was noticed. The patient was found to be suffering from slight mitral stenosis, and the urine contained a small quantity of albumin; there was an incomplete right hemiplegia, flaccid in type, with no involvement of sensation, the knee-jerks were just present, and the plantar reflex was of flexor type. The case was diagnosed as one of mitral stenosis, and the hemiplegia looked upon as dependent on embolism, and the case was treated with a rigid milk diet. The patient survived until May 16th. On that day Cheyne-Stokes respiration set in, and later on epileptiform convulsions, localized to the right arm and accompanied by loss of consciousness. Contraction of the pupil was well marked, the convulsive seizures were frequently repeated at short intervals, the patient not recovering consciousness, and death occurred at midnight. At the post-mortem the heart was found hypertrophied, the mitral orifice was narrowed, the kidneys were small and granular, and on stripping the capsule was unduly adherent. No infarcts were present. The vessels at the base of the brain were normal, and the cerebral hemispheres, pons, and medulla did not show any evidence of cerebral hemorrhage or softening, either recent or old.

Both these cases are very remarkable, especially, owing to the long duration of the cerebral symptoms. As Brodier points out, in the first case the incomplete hemiplegia, which developed progressively in a patient suffering from cardiac hypertrophy and renal disease, seemed to eliminate uræmia as the cause of the palsy, and in the second case the existence of mitral stenosis seemed to allow of no doubt as regards the nature of the cerebral lesion. Brodier mentions that Rendu and Bodin have recorded a somewhat similar case where a motor aphasia and a brachial monoplegia of sudden onset in a patient suffering from a systolic aortic murmur gave rise to a diagnosis of embolism, but where, apparently, the trouble was uræmic.

Brodier points out that uræmic hemiplegia rarely supervenes in cases of apparent good health. It is more usual for the hemiplegia to be

preceded by symptoms drawing attention to the renal trouble. In both Brodier's cases this was so : in one the patient had presented symptoms for two years, and in the second for five or six years. Hemiplegia, according to Brodier, when of uræmic origin, is usually flaccid during the whole of its duration, and the motor palsy is usually incomplete, and sensation is not affected. Further, the hemiplegia of uræmia is generally transitory ; thus Brodier quotes one case recorded by Letulle, which lasted twenty-five days, another of thirty days' duration, and another of two months. It is certainly extraordinary that in Brodier's cases the duration was in one case thirty-eight months, and three years in the second. Further, in most cases of uræmic hemiplegia, one of the most characteristic features of the condition has been the variation in the severity of the symptoms from time to time. In this respect, however, Brodier's cases were exceptional. In twenty-nine cases out of thirty-seven quoted by Baillet no gross lesion was found.

It has been supposed that the cause of uræmic palsies was more or less localized cerebral œdema ; but this view has never received very general acceptance, owing to its inconstancy in the post-mortem, and Brodier was unable to find in his cases any evidence of such a condition. Similarly the lesions in his cases could not be dependent on atheromatous or other changes in the walls of the vessels, as especially in Case II. the vessels were perfectly healthy. Some writers have considered that spasm of the cerebral vessels might give rise to the uræmic palsies, but this also is not a satisfactory explanation for palsy lasting so long, and Brodier is inclined to think that they must depend on important histological lesions of the nerve cells. He concludes that uræmic hemiplegia might, in exceptional instances, last for several years, and that it is not accompanied by any trophic or vasomotor trouble in the paralyzed limbs, and that death usually supervenes as a result of other uræmic symptoms. He emphasizes the point that where hemiplegia is accompanied by chronic albuminuria the possibility of the lesion being dependent on chronic uræmia must be borne in mind, although, in many such cases, the cerebral lesion may be of vascular origin. Finally, he considers that the presence of a hemiplegia of some duration in a patient suffering from chronic Bright's disease may be looked upon as of uræmic origin when the knee-jerks are not exaggerated, Babinski's sign is absent, and there are no trophic or vasomotor complications.

Although, as stated above, the effects produced by uræmia are extremely various, they are most of them dependent on disturbance of the functions of the cortex of the brain. What may be called bulbar symptoms are not common, with one notable exception, viz., the disturbance of respiration that is such a constant phenomenon in uræmia.

Respiratory distress may be, perhaps, considered the most constant uræmic symptom, and this is not only true in cases of acute uræmia, but also in the subacute and even in the chronic. Although disturbance of respiration, whether of a Cheyne-Stokes character or of another form, is so frequent, symptoms dependent on the disturbance of the activity of the other bulbar centres are occasionally seen, but are by no means common. Londe¹ has recently recorded such a case. The patient was a woman, aged forty-two years, who came under observation with albuminuria and *morbis cordis* in 1900. She had as a girl suffered from mitral stenosis, and one of her confinements (1882) had been accompanied by albuminuria, together with headache and some dyspnœa, but no eclamptic fits. She remained in a fair state of health until 1898, although she had suffered from pericarditis in 1891. During the last few years she had been put on a milk diet from time to time, and had improved considerably; but in the autumn of 1900, having relaxed the diet, she became a good deal worse, suffering from weakness and dyspnœa and diarrhœa. In addition, some loss of flesh had occurred, and she suffered from so-called indigestion. Sleep was poor, and it was not at all infrequent for her to awake suddenly in distress, with great shortness of breath, which subsequently became of the Cheyne-Stokes type. The respiratory distress was of a somewhat peculiar type, inasmuch as it took the form of a sensation of suffocation, with considerable dyspnœa, causing the patient to assume a sitting posture. These sudden attacks of suffocating dyspnœa were accompanied with nausea and a slight cough, the expectoration was slightly mucoid, and was insignificant in amount. On auscultation a few râles were found at the apex of the lungs, which disappeared rapidly with the subsidence of the choking. These attacks lasted generally about an hour, and during the height of the seizures well-marked tachycardia was present, the pulse rising from a normal of 80 to 90 pulsations to 120. The patient passed about 1500 c.c. of urine of a specific gravity of 1010 and containing from 1 to 4 grammes of albumin, in some cases amounting to as much as 7 grammes. She excreted some 17 or 18 grammes of urea in the twenty-four hours. Londe also calls attention to the fact that in addition to these physical symptoms the patient had some psychical disturbance, such as a persistent presentiment of impending death and visions of her dead mother.

Psychical symptoms are not uncommon, as is well known both in cases of renal disease, and also in cardiac cases. During the subsequent course of the malady the patient not only suffered from those mentioned above, but, in addition, had great mental depression associated with

¹ Assoc. Méd. des Hôp. de Paris, 1901, No. 24.

somnolence and followed by delirium and hallucinations. The attacks of dyspnœa accompanied by tachycardia were at first relieved by a rigid milk diet, but subsequently returned, and became especially marked in the morning. All these uræmic manifestations were marked at a time when the secretion of the urine was still abundant. In the early part of 1891 the paroxysms of dyspnœa not only occurred in the morning, but also during the day, and the patient suffered from cramps and transitory amblyopia and great sleeplessness; a suppository containing small quantities of opium produced relief. As the attacks of dyspnœa became more severe the patient tended to assume a sitting posture, which she was unwilling to depart from, and the author draws attention to the attitude of marked flexion which she thus assumed. At this time delirium was a marked feature, and she also had transitory delusions of persecution; terrifying hallucinations were also frequent. The paroxysms of dyspnœa continued to be present, but in the middle of April a complication occurred of a very sudden and copious intestinal hemorrhage, which was sufficient in amount to cause fainting. This copious intestinal hemorrhage recurred once again later on. The Cheyne-Stokes rhythm became more marked and persisted during sleep. During a state of wakefulness the period of dyspnœa in the Cheyne-Stokes rhythm was accompanied by movements on the part of the patient, who threw her head back and opened her arms. During the period of apnœa these movements ceased, and she assumed the same sitting posture described above. Londe also draws attention to the fact that there was a waxing and waning of consciousness *pari passu* with the dyspnœa, and that remarks addressed to the patient during the period of apnœa were not followed by any answer. Toward the termination of the illness some dysphagia was present, and the palate contracted badly, but was never sufficiently involved to cause nasal regurgitation.

There are points of interest about this case, although many symptoms are such as are well known in uræmia. The most striking features, as the author himself points out, are the bulbar symptoms, viz., the paroxysms of dyspnœa associated with tachycardia, and followed by some labio-glossal laryngeal weakness. The most perfect form of Cheyne-Stokes respiration is not uncommonly seen in uræmia, and, according to the experience of the writer, it is accompanied frequently by other periodical disturbance, such as variations in the frequency of the pulse, in the degree of the contraction of the pupil, and in the activity of the motor and psychical functions of the brain. In the complete form of the disease the patient presents not only an increase and diminution in the activity of the respiratory movements, but, more or less synchronously, with an increase in the respiratory acts the pupils dilate, the pulse becomes quickened, the activity of the psychical centres

increases, and movements of varying degrees of purposefulness are produced. The disturbance of the higher cerebral centres is sometimes sufficient to lead to unconsciousness during the periods of apnoea, consciousness being only intermittently present during the dyspnoea. This periodic disturbance in the activity of other cerebral centres would seem to show that the pathology of Cheyne-Stokes respiration cannot be associated entirely with the disturbance of bulbar centres. It is not a peculiarity of Cheyne-Stokes respiration produced by uræmia to be accompanied by these other manifestations; they may be seen both in the cardiac form and in the cerebral form, but they are often more perfectly marked in uræmia than in the others. Another important point to which attention is drawn by Londe is the fact that small doses of opium are efficacious in relieving the dyspnoea of uræmia (0.05 gramme to 0.1 gramme of powdered opium in the form of a suppository).

The question of withholding or giving opium in renal disease is often one of considerable difficulty. This question should not be determined by the mere presence of albuminuria, a far more important point is the presence or absence of pulmonary complications. Opium is far more dangerous in conditions of respiratory embarrassment dependent on mechanical causes, such as the presence of hydrothorax or the presence of copious mucoid fluid in the bronchial tubes. Under these circumstances the dulling of the activity of the respiratory centres by opium may produce very serious, if not fatal, effects. On the other hand, if the dyspnoea arises from the action of toxic substances on the nerve centres, and where there are no mechanical conditions embarrassing the respiratory act, opium may be of great value. The old opinion against prescribing opium in cases of renal disease, owing to the supposed inefficiency of the kidney to excrete, is not one that is borne out by experience, although most physicians would agree that on the whole the administration of opium in renal disease is more dangerous than in health, but this often arises from the presence of pulmonary complications such as those mentioned above. Opium and its alkaloids are excreted mainly by the alimentary canal, rather than by the urine, and, therefore, inefficiency in the excretory activity of the kidney is not of such moment as at first sight might seem. Opium, however, is extremely dangerous in the treatment of some forms of uræmia where the toxic condition is complicated by the presence of pulmonary complications, as, for instance, pulmonary œdema or hydrothorax.

Londe's case is also of interest from the marked development of the psychical symptoms.

Londe is inclined to attribute the intestinal hemorrhage, which was a marked feature of his case, to mere vasomotor dilatation. In the absence of a post-mortem examination, it is perhaps justifiable to sus-

pect that the condition may have been due to the presence of intestinal ulceration as ulcerative colitis, and other forms of intestinal ulceration are not very uncommon in cases of renal disease. As Londe points out, the fact that the blood was passed in the form of *melæna* was to a certain extent an argument against the ulceration being in the lower part of the large intestine, but it does not exclude the presence of ulcers higher up.

Although uræmia in its various forms is associated with most organic diseases of the kidney, and although any form of uræmia may occur in any of these different organic diseases, yet there seems to be some tendency for the association of definite clinical types of uræmia with certain diseases of the kidneys. This is especially seen, for instance, in the association of latent uræmia, with calculous and other forms of obstruction, and, also, though perhaps not quite to the same extent, in the form of uræmia, which accompanies consecutive nephritis, and in that seen in bilateral hydronephrosis. The more severe forms, such as the comatose and the eclamptic, are not usually seen in these chronic diseases, and this is more especially so in consecutive nephritis and bilateral hydronephrosis. This, however, is not dependent on the maladies being chronic ones, as is shown by the fact that some of the most violent forms of uræmia may be seen in the granular contracted kidney and in other forms of chronic Bright's disease. In cystic disease of the kidney uræmia is also a frequent complication, and here it not uncommonly assumes the latent type in a more or less modified form, although sometimes the eclamptic variety is seen in this disease. Some authors, especially the French, have coined the word "*urinémie*" for the toxic state associated with conditions in which there is obstruction to the ureters, as in some forms of calculous disease, and in carcinoma and other diseases of the uterus, and, more especially, in conditions of bilateral hydronephrosis following an obstruction of the lower urinary tract.¹ Revilliod draws attention to the very obscure form in which the uræmia manifests itself in these cases, and he records an instance of a patient who was admitted for digestive, respiratory, and nervous symptoms, which, although they pointed to the existence of a grave toxic state, were not immediately recognized to be of uræmic origin. The patient was a man, aged forty-four years, who, after suffering from typhoid fever at the age of twelve years, remained in good health until approximately a year before his death. Prior to the last illness he had not suffered from any symptoms referable to the urinary tract. Six months before his death he began to suffer from giddiness and weakness. He had followed the occupation of a painter, and was supposed at this time

¹ *Revue Médicale*, March, 1901.

to be suffering from lead-poisoning. Emaciation soon became a marked feature, and he began to suffer from respiratory distress, and ultimately from extremely severe dyspnoea. On admission, dyspnoea was a most prominent symptom, the respiratory movements being deep and prolonged, but not accelerated; and it is especially stated that the rhythm was a normal one. The deep respirations were accompanied by a very considerable amount of air-hunger; there was no cough and no expectoration. The appetite was poor, the tongue was tremulous and covered with a brownish-gray fur, and the breath offensive, although there was no lead-line. There was a certain amount of meteorism, and some diarrhoea. The cardiac impulse showed equivocal signs of hypertrophy, and the sounds were distinct, but no murmur was present. The patient was pale, but presented no oedema. He showed no symptoms directly referable to the urinary system, except that there was some irregularity in micturition, and the quantity of urine secreted was considerable. The urine was of low specific gravity, 1007, and contained traces of albumin. Subsequently the diarrhoea became more marked, vomiting set in, and the temperature became subnormal. The dyspnoea and air-hunger remained throughout marked features of the patient's illness. The dyspnoea was so marked as to suggest the diagnosis of uræmia, but this was at first sight not considered probable, owing to the absence of definite signs pointing to the existence of cardiac hypertrophy, and there were no signs of increased arterial tension. The dyspnoea gradually increased, and extreme cachexia developed.

At the post-mortem strictures of the urethra were found, the bladder was hypertrophied, and the ureters distended. The kidneys presented the following appearances: the capsule was adherent, the organ was somewhat increased in size, and the surface irregular and pale. On section the renal substance was pale, small in amount, and there was no distinction between the cortex and the medulla, the renal pelvis was distended, and the mucous membrane slightly hyperæmic. In other words, there was a bilateral hydronephrosis, without any septic complications.

Revilliod points out that the interest of his case rests mainly in the fact that as there were no inflammatory lesions, the patient suffered from the effects of an intoxication caused by the excretory substances present in the urine. He draws attention to the fact that it is usual to consider that in such cases marked cardiac effects, such as arrhythmia and a galloping rhythm, together with oedema and Cheyne-Stokes respiration, are generally present. In his patient, however, none of these symptoms were present; but, on the other hand, vomiting and diarrhoea were well marked, together with an extremely rapid loss of flesh, and, in the later stages of the illness, a number of furuncles developed in the skin. He considers that the most character-

istic symptoms were the weakness, the loss of flesh, exaggeration of the deep reflexes, the great dyspnœa, together with the diarrhœa and vomiting. It is noticeable that in this patient, as in so many others, the history failed to throw any light on the case, as no symptoms referable to the urinary system were elicited, and that, although the patient had evidently suffered from stricture for many years, this had apparently not produced any very great inconvenience. This latency of the symptoms produced by the underlying chronic disease is one of the conditions which give rise to the greatest difficulty in the diagnosis of this and other forms of latent uræmia.

A clinical picture such as that described in Revilliod's patient is not only seen in cases of uræmia following on bilateral hydronephrosis, the result of disease of the lower urinary tract, but also in certain cases of congenital anomalies in the kidneys. Three such cases have fallen under the observation of the writer where a hydronephrosis, apparently of congenital origin, had existed for a number of years, varying from eighteen to twenty-five years, without producing any marked symptoms except frequency of micturition, and also incontinence dependent on some anomaly of the lower urinary tract, although the post-mortem examination in all three cases failed to clear up definitely the actual cause of the incontinence. In all these three cases the hydronephrosis was slight in amount, the pelvis of the kidney and the ureters being dilated, the kidneys themselves not being greatly distended, but considerably deformed in shape, and containing very little true renal substance. All three of these patients came under observation, and died with symptoms very similar to those recorded by Revilliod. Wasting and vomiting were marked phenomena, and as the disease approached its fatal termination dyspnœa became more and more obvious, and, like that described in Revilliod's case, it was characterized more especially by the depth of the movements and by air-hunger than by any profound alteration in the rhythm, of the nature of Cheyne-Stokes respiration. In one of these cases the incontinence of urine was such a marked feature that at first sight the case was looked upon as one of disease of the spinal cord. It would seem, from these and other cases, that a classification of the different forms of uræmia associated with different structural diseases of the kidney may, to a certain extent, be possible. First, acute and fulminating uræmia are probably most often associated not only with acute nephritis, but more especially with that form of chronic Bright's disease in which the kidneys are granular, but where the lesion is primarily a renal one, and not the mere development in the kidney of the effects of a general arterio-sclerosis. Subacute uræmia, characterized by a certain amount of vomiting, diarrhœa, cramps, twitchings, hiccough, and Cheyne-Stokes respiration, is more especially seen in that form of chronic Bright's

disease which is accompanied by dropsy, the so-called large white kidney, or chronic parenchymatous nephritis. A latent uræmia, in which the patient presents no symptoms except a gradually increasing weakness, contraction of the pupil, and a subnormal temperature, is especially associated not only with cases of calculous suppression, but also with other forms of complete suppression, occurring in patients who have not got long-standing chronic destructive diseases of the kidney. Thus this clinical picture may be seen in cases of sudden occlusion of the renal arterioles, and also in some cases of reflex suppression, and even in some forms of toxic suppression, *e. g.*, diphtheria.

This, on the whole, is the most remarkable form of uræmia, and even in the cases where it is dependent on calculous obstruction there is no retention of urine above the obstruction, it is really associated with the development of a true suppression. In cases where there is not only obstruction but also urinary retention, as, for instance, in the case described by Revilliod, and in the cases of bilateral hydronephrosis associated with carcinoma of the uterus, the clinical picture is somewhat different. Here diarrhœa, vomiting, and dyspnœa are much more urgent and prominent symptoms than in the true latent uræmia associated with calculous obstruction, and the patient presents much more frequently a cachectic appearance, and is much more obviously profoundly ill than in the cases associated with calculous anuria. It is not surprising that the symptoms should be slightly different in the two cases, seeing that in the one the urine is elaborated but cannot be excreted, whereas in the other there is complete suppression without any actual formation of the urinary elements.

Finally, in cystic disease of the kidneys it would seem as if the uræmic phenomena fall into one of two groups: either the patient presents the symptoms of a latent uræmia, somewhat similar to that seen in calculous suppression, or else in this condition a violent epileptiform or eclamptic uræmia may be seen.

The above statements can only be looked upon as a general summary of the condition, and there can be no doubt that frequently there are many exceptions to the association sketched above of different types of uræmia with different organic diseases. It is especially important to bear in mind the latency of the symptoms of the original chronic disease that is giving rise to the terminal symptoms of uræmia, because otherwise the nature of such cases may be quite overlooked. In many forms of uræmia associated with chronic destructive diseases of the kidney it is by no means uncommon for the patient to present no marked symptoms of ill-health until the development of the terminal and fatal complication.

CARDIAC HYPERTROPHY AND RENAL DISEASE.

Cardiac hypertrophy, as is well known, is a frequent accompaniment of renal disease, and more especially of certain forms of it. Although a frequent accompaniment of many diseases destroying the renal parenchyma, cardiac hypertrophy is not an invariable phenomenon even in those forms of renal disease which are most frequently associated with it. This is one of the many reasons which have caused such great differences of opinion among pathologists as to its nature.

Cardiac hypertrophy is especially well marked in the contracted or atrophic form of Bright's disease, and also in granular kidney. It is, however, not uncommonly just as well marked in cases of ordinary chronic Bright's disease dependent on the presence of the so-called large white kidney, and sometimes it is of such rapid development as to be well marked in cases of acute Bright's disease, some six weeks after their origin. Although cardiac hypertrophy is especially associated with chronic Bright's disease and with the granular kidney, yet both these maladies may reach a high degree of development, and even cause death, without the occurrence of any notable cardiac hypertrophy, and it is more or less to this branch of the subject that Bouveret¹ devotes himself. Traube, who called attention to the relationship of cardiac hypertrophy and renal disease, observed that even in interstitial nephritis there was some 7 per cent. of cases in which no marked cardiac hypertrophy occurred, that is to say, in that form of renal disease which is most likely to be accompanied by cardiac and arterial changes. The non-occurrence of cardiac hypertrophy in some forms of granular kidney was thought to be dependent on the presence of some other underlying condition which interfered with the hyperplasia of the heart, such as tuberculosis, or the presence of some cachexia, or even mere senility. Bouveret draws attention to the fact that there must be some other factors at work, inasmuch as cardiac hypertrophy may be absent in young persons suffering from granular kidney or from the atrophic or contracted form of Bright's disease without the presence of any general cachexia, and in the absence of tubercle. Bouveret quotes the case of a girl, aged twenty-two years, who had had good health up to the age of puberty, and then subsequently to that had become anæmic and had suffered from palpitation and excessive losses at the catamenial periods. Soon after this she began to suffer from œdema of the face, and subsequently of the feet, and later she noticed that her sight was impaired, she then began to suffer from thirst, and passed a considerable quantity of urine; epistaxis was also marked at this time. The patient when

¹ Lyon Médical, 1901, vol. xcvii., No. 27.

admitted was suffering from considerable anæmia, was extremely weak, and had slight œdema of the face and feet. In addition to these, cramps of the arms and legs were present. The pulse was not of high tension, and the heart was apparently not enlarged. The urine was of low specific gravity, 1009, and contained a large quantity of albumin. Ophthalmoscopic examination showed the presence of œdema in both papillæ. Soon after the patient's admission the quantity of urine excreted underwent diminution, and on the fifth day she died of uræmia. At the post-mortem examination the heart was found not hypertrophied, and it weighed 255 grammes. The kidneys were small, pale, gray, tough, and fibrotic, the right one weighed 60 grammes and the left 25 grammes. The aorta was described as narrow, like that described by some writers as characteristic of chlorosis. This case recorded by Bouveret would seem to be one falling under the category of the contracted white kidney, quite different both in its morbid anatomy and in its clinical course from the true granular or raspberry kidney. This is shown by the fact that the kidneys were very small, pale in color, and that during life the urine contained a considerable quantity of albumin. Further, the case is characteristic in the fact that the malady was extremely insidious in its onset, and the patient died with some suddenness from uræmia. As the writer¹ has stated, he is of the opinion that this form of renal disease constitutes a definite group, characterized not only by the morbid anatomy, but also more especially by its clinical course. The fact that in several of these cases the cardiac hypertrophy was absent affords further evidence of the difficulty of accepting Traube's explanation of the mode of development of cardiac hypertrophy in renal disease. Traube considered that the diminution in the amount of renal substance was followed by an increased blood pressure of vasomotorial origin to compensate for the loss of renal substance, and this, together with hydræmia, led to such a permanent increase in the blood pressure as to bring about the cardiac hypertrophy. Many of these cases of contracted white kidney occurring in young adults, and, perhaps, especially in young women, are instances where the destruction of renal substance is as great, if not greater, than that seen in the granular kidney and in other forms of renal disease; and yet, although cardiac hypertrophy is often present, and even in considerable amount in such cases, yet, as Bouveret's case and others like it show, it is by no means an invariable accompaniment. There are, however, other reasons for thinking that cardiac hypertrophy cannot be, as Traube thought, dependent on the mere destruction of renal tissue. There are other kidney diseases where, notwithstanding very great

¹ Clinical Varieties of Bright's Disease, *Lancet*, 1900.

destruction of renal substance, no cardiac hypertrophy ensues. Such illustrations are afforded by cases of hydronephrosis, and more especially by some cases of congenital hydronephrosis, and other malformations of the kidney seen in the young and not necessarily rapidly fatal. This is more especially true of cystic disease.

In all of these conditions cardiac hypertrophy is usually absent, although in some cases of cystic disease, where the remaining renal tissue scattered between the cysts has undergone fibrotic changes, some cardiac hypertrophy may be present. It is not uncommon to find cases of malformation of the kidney of various kinds, especially hydronephrosis and dilatation of the renal pelvis and ureters, where, either owing to the mere malformation or else to the secondary processes liable to attack such malformations, the renal tissue is very greatly diminished in amount and yet no cardiac hypertrophy is present. Such patients often live for many years, and there is, therefore, ample time for the development of cardiac hypertrophy. Further, there is no experimental evidence in favor of the view that diminution of the renal substance brings about cardiac hypertrophy. In Bright's disease, as is well known, a moderate amount of cardiac hypertrophy may be brought about in a few weeks. On the other hand, the removal of two-thirds of the total kidney-weight in animals may fail to lead to the production of any cardiac hypertrophy, notwithstanding the fact that the animal may live in good health after such mutilation for months, and even for as long as two years. Even in cases of the true granular kidney the degree of cardiac hypertrophy is not necessarily associated with the extent to which the renal lesion is advanced, and it is not uncommon to see instances of extreme cardiac hypertrophy associated with the granular kidney and general arterial sclerosis where the renal lesion is comparatively speaking slight. Bouveret associates the absence of cardiac hypertrophy in his case more especially with the presence of chlorosis and a vascular aplasia. The association of chlorosis with vascular anomalies, and more especially with a want of development of the aorta, and a general vascular aplasia, is the view that has always received most support from Continental writers, and the presence of chlorosis in many cases of contracted kidney is a fact that all clinicians would agree to. It is not unusual in the experience of the writer for such forms of renal disease to come under observation not only with chlorotic symptoms, but with no other symptoms, the renal lesion, severe as it is, being latent. Such cases are readily overlooked unless a routine examination be made of the urine and of the fundus oculi. Albuminuric retinitis is very frequently present in such cases, and the urine as mentioned above is usually characterized not only by its abundance and low specific gravity, but also by the presence of very con-

siderable quantities of albumin, sometimes as much as a third or more, usually a sixth or a quarter. Bouveret in his paper has collected a number of cases of so-called interstitial nephritis with absence of marked cardiac hypertrophy, although no other case, except the one described above, has fallen under his observation. He collects some seventeen cases, in all of which tuberculosis or the existence of any cachexia is excluded, and all the patients at time of death were under thirty-five years of age. In only five of the seventeen cases, however, has the weight of the heart been accurately determined, and in three of these there is no hypertrophy, and in the other two the increase in weight is so slight as to scarcely merit the term of hypertrophy. It is noteworthy that in the cases occurring in young women the record is often made that the aorta was narrow.

Although these records are in many respects imperfect, they show that cardiac hypertrophy is by no means an invariable accompaniment of the contracted form of Bright's disease.

Another point which is brought out by many of these cases is the fact that, apparently, cases of contracted kidney or chronic Bright's disease in which cardiac hypertrophy does not occur tend to run a very rapid course, and also, according to Bouveret, to be complicated by uræmia, and he considers that this, perhaps, may be dependent on the fact that the cardiac hypertrophy of renal disease may in some measure be of advantage to the patient.

The occurrence of uræmia in cases of the contracted form of chronic Bright's disease is undoubtedly a clinical fact of great importance. It may be, perhaps, correlated rather with the nature of the renal lesion than with the absence of cardiac hypertrophy, since it is unquestionable that in the majority of such cases cardiac hypertrophy is well marked, and, in fact, its presence and the presence of general arterial degeneration afford frequently means of recognizing the existence of the underlying grave renal disease. The existence of this form of Bright's disease has more than once been diagnosticated owing to the characteristic changes in the pulse or in the vessels of the fundus oculi.

Many writers have described cardiac hypertrophy as existing in a slight form in cases of chlorosis, so that it is difficult to admit that the coexistence of chlorosis with the renal lesion is the cause of the want of development of the cardiac hypertrophy.

The high tension of renal disease is certainly of doubtful advantage to the patient, even if it be the cause of maintaining a comparatively free secretion of urine. For not only may it be followed by some of the most serious consequences, such as cerebral hemorrhage, but it often of itself gives rise to great distress in causing headache and sleeplessness. Most practitioners would look upon the high tension of renal

disease as one of the conditions which calls for treatment directed to lowering the tension.

Croftan¹ also deals with the question of the cardiovascular changes in nephritis, but from an experimental stand-point. He considers that Traube's mechanical theory of the production of high tension is disproved, owing to a variety of reasons, more especially because Ludwig showed that ligature of both renal arteries failed to raise the arterial pressure, and because cardiac hypertrophy is most developed in that form of interstitial nephritis, viz., the glandular kidney, where the increased excretion of water is most marked, and, therefore, that there would be no reason for supposing that the renal lesion had brought about any condition of hydræmia or of hydræmic plethora. Croftan considers that the alternative hypothesis that cardiac and arterial changes are brought about by toxic substances is the more probable one. Obliteration of the renal arteries by ligature, however, is not really comparable to the diminution of the calibre of all the branches of the renal arteries brought about either by vasomotor excitation or by narrowing of the lumen of the vessels. It is obvious that diminution in the calibre of the minute arterioles, particularly in an organ so vascular as the kidney, might appreciably affect the blood pressure when the ligature of the main artery would not. It is also conceivable that impulses may pass from the kidney capable of affecting the vasomotor system, as experiments have shown that excitation of the central end of the renal nerves is capable of producing a very great increase in the blood pressure. In this respect the renal nerves are not peculiar, but yield results similar to those obtained by stimulation of other nerves containing afferent fibres distributed to the abdominal viscera, and this is a fact which, perhaps, has not received sufficient attention in discussions in regard to the mode of production of high tension. In the opinion of the writer it is quite possible that afferent impulses may pass from the kidneys and other viscera to the vasomotor system, which might conceivably lead not only to transitory but to permanently increased high tension. However this may be, it is certain, as mentioned above, that the increased tension cannot be correlated with any diminution in the amount of the available renal substance, and, therefore, in default of any other explanation, we are thrown back on the view that it is brought about by the circulation of some toxic material in the blood.

The view that the cardiac and vascular changes might be dependent on the action of some toxic substance present in the blood is one that dates from Bright himself, who considered that in nephritis excrementitious substances were present in the blood in excess. This view has

¹ American Journal of the Medical Sciences, vol. cxx., No. 5.

never met with the general and wide-spread acceptance that was at one time accorded to Traube's hypothesis, although certain pathologists, from time to time, realizing the difficulties in the way of accepting Traube's views, have fallen back on the older explanation. Thoma has accepted or has long held the view that the cardiovascular changes in renal disease might probably be of toxic origin. There has, however, been great discrepancy among different authors as to whether the cardiac hypertrophy or the arterial lesion is the primary morbid change. According to some it has been supposed that the toxic substance retained in the blood has caused a more or less marked arterial constriction, and that the increase in the blood pressure brought about in this way has led ultimately to an hypertrophy of the heart. Others have supposed that the primary action of the toxic substances was on the heart itself, and that the vascular lesions have really developed secondarily to meet the increased strain thrown on them by an increase in the activity of the heart. In the one case the arterial lesions would be primary, in the other secondary, to meet the increased strain thrown on them. There are many toxic substances which are capable of producing vascular lesions by altering the endothelium ; but, after all, the prominent vascular lesion present in renal diseases is the thickening of the subendothelial coat of the arteries, although it may not be the sole one. This thickening of the subendothelial coat is not only shown by the increased amount of fibrous tissue, but also by the presence of a greatly increased amount of elastic tissue, and it is no uncommon phenomenon for this subendothelial coat to equal in thickness all the other coats of the artery together. It is easier to regard such a thickening as a result of increased blood pressure than to look upon it as a primary effect produced by the action of a toxic substance.

It is possible the increase in the arterial pressure which has been so often observed clinically in renal disease may be brought about by an increase in the functional activity of the vasomotor system ; but it is difficult to believe that such persistent result could be caused by the circulation of toxic material in the blood, as it is almost universal for poisons, even if they produce a large initial effect, to lose more or less quickly their typical action. In other words, it is difficult to believe that the circulation of toxic substances in the blood is capable of producing such a persistent functional increase in arterial pressure as to cause the thickening of the arterial coat in response to it. At the same time, although difficult of acceptance, it may be that such a view is correct. These and other difficulties have led pathologists to think that it is possible that the increase in the arterial tension may be brought about primarily by increased cardiac action. There are only three ways in which the blood-pressure can be affected : (1) by an increase in the

activity of the heart ; (2) by increased peripheral resistance, and (3) by an increase in the amount of the fluid in the bloodvessels. As mentioned above, it is difficult to believe that the action of a poison could cause a persistent increase in the peripheral resistance dependent entirely on an increase in the functional activity of the vasomotor system. Even such a substance as the suprarenal extract, which produces very great effects upon the vasomotor system, is one that is weakened by repetition, although it must be confessed that the discovery of this substance might be used as an argument in favor of the normal blood-pressure being partly dependent on the maintenance of a toxic constriction produced by chemical agents. It is difficult to correlate the heightened tension of renal disease with the variation in the fluid contents in the vessels, inasmuch as this high tension is seen both in those forms of renal disease accompanied by dropsy and a scanty secretion of urine, and in those where dropsy is absent and an abundant urine is secreted.

We are thrown back on the view that the heightened tension of renal disease may be brought about by the action of a toxic substance perhaps on the heart, perhaps on the peripheral vessels. A number of observers have searched for such a substance in the urine, and the injection of urea into the bloodvessels has produced in the experience of many investigators a rise in blood pressure and an increase in the activity of the heart. Croftan records in his paper that Ustimovitch, Grutzner, and others have obtained not only a rise of blood pressure, but also arterial constriction, and Israel has claimed that he has produced hypertrophy of the heart by the administration of considerable quantities of urea for prolonged periods. Urea is undoubtedly present in the blood in great excess in many cases of renal disease even at a time when uræmia is absent. Thus the percentage in the blood may be doubled or quadrupled quite apart from the presence of any marked uræmia, and in this latter condition as much as twenty times the normal, or even more, may be present according to observations made by the writer. Croftan concludes from his experiments that uric acid is without effect upon the blood pressure, the arteries or the heart, but that the same is not the case for the other alloxur bases present in the urine, more especially xanthine and hypoxanthine, and he conducted a number of experiments in which quantities of xanthine and hypoxanthine were injected into normal rabbits. He claims that not only do these substances produce a nephritis varying in amount with the quantity injected and the frequency of the injections, but also that xanthine and hypoxanthine are capable of increasing the blood pressure. Taking the normal blood pressure of the rabbit as from 60 to 90 mm. of mercury, the injection of xanthine was followed by a rise of pressure to as much as 109 mm. The increase in pressure was not only observed

immediately after the injection, but persisted, so that, for instance, in one experiment where xanthine was injected for a period of six weeks, the pressure was as high as 108 mm. on the forty-second day and twelve hours after the last injection. Other experiments extending over a more prolonged period were attempted, and more especially one where xanthine, in a dose of 1 c.c. of a $\frac{1}{2}$ per cent. solution, was injected twice daily for a period of six months. In this animal the heart is described as having undergone great hypertrophy, and Croftan also describes atheromatous changes consisting of small-celled infiltration of the intima and adventitia, together with thickening of the intima. He considers that xanthine and hypoxanthine are capable of producing a rise in arterial pressure which may be due to arterial spasm, increased heart action, or both. He further considers, inasmuch as changes in the inner coat are produced by the continued action of these substances, that the alloxuric bases cause primarily an arterial spasm, and that this leads to an increase in the activity of the heart, and that the vessel walls undergo a thickening to meet the increased strain so produced. There can be no question, if these observations are confirmed, that a very considerable amount of light will be thrown on the pathology of increased tension, and a great advance will be made if it can be definitely proved that such a result was dependent on the action of definite chemical substances. There are, however, difficulties in the way of accepting the view that the cardiovascular changes of renal disease are dependent on the action of a toxic substance that is retained in the organism owing to deficient excretion. It is, moreover, probable that in renal disease toxic substances may be present in the blood and their origin due not so much to retention but rather to altered metabolism. Both experiment and pathology point to the conclusion that in renal disease there is great and excessive wasting of the proteid tissues of the body, and it is by no means improbable that toxic substances formed as a result of anomalous proteid metabolism may be present in the blood and even in large quantity. There is no inherent improbability that such substances as xanthine and hypoxanthine may be formed in increased abundance as the result of altered proteid metabolism. If we do not look upon all the toxic substances present in the blood in renal disease as dependent on retention and diminished excretion, but broaden our view and consider that some may arise from increased production, some of the difficulties in the way of looking upon cardiovascular changes as dependent on a toxic cause might disappear.

PHYSIOLOGY.

BY ALBERT P. BRUBAKER, M.D.

GENERAL PHYSIOLOGY.

THE physiological work of the past year has been in no wise startling, and scarcely anything new of value has been brought forward. The great majority of investigations are simply confirmatory of or antagonistic to previously asserted details. The Hull Laboratory of Chicago, however, must be complimented on the continuance of its activity, and it is with pleasure that we review its work.

Experiments on Artificial Parthenogenesis in Annelids (*Chætopterus*) and the Nature of the Process of Fertilization. In Loeb's own words¹ the following is the problem which he undertook to solve: "My preceding papers on artificial parthenogenesis had proved that by an increase in the osmotic pressure of the sea-water the eggs of many, if not all, echinoderms can be caused to develop parthenogenetically. Two new problems presented themselves for immediate consideration. The one was to raise the parthenogenetic larvæ until they were sexually differentiated in order to decide whether or not they are of uniform sex. The second problem was to try whether artificial parthenogenesis is confined to the group of echinoderms or whether it is a more general phenomenon. As the means for the raising of sea-urchins were not available at Wood's Holl this year, the former problem had to be postponed. The solution of the second problem, however, was possible, and yielded the result that the unfertilized eggs of *Chætopterus*, a marine annelid, can be caused to develop into swimming ciliated larvæ (trochophores)."

These experiments, similarly to those of last year in reference to the sea-urchins, were carried out in large numbers and with every care to provide against contamination by spermatozoa. Their success can scarcely be doubted since the control experiments invariably showed negative results. From them he concludes:

The unfertilized eggs of *Chætopterus* do not reach the trochophore stage if left in normal sea-water, provided the proper precautions are

¹ American Journal of Physiology, 1901, vol. iv. p. 423.

taken against contamination by spermatozoa. Such eggs show no change during the first seven or nine hours, but may begin to segment after that time. In such cases the segmentation, as a rule, does not proceed beyond the two to four-cell stages, but may in exceptional cases go as far as the twelve to sixteen-cell stages. We may say that *Chætopterus* possesses a higher degree of parthenogenetic tendency than the *Arbacia* egg, which begins to segment later, after about twenty hours, and does not proceed beyond the two to four-cell stage.

The unfertilized eggs of *Chætopterus* are able to develop into swimming trochophores if they are placed for about one hour in one of the following solutions, and then put back into normal sea-water :

1.	15-20	2½ n	NaCl	+ 85 sea-water.
2.	40	2 n	cane sugar	+ 60 sea-water.
3.	30	2½ n	MgCl ₂	+ 70 sea-water.
4.	10	5 n	CaCl ₂	+ 90 sea-water.

All these solutions have one element in common, namely, the about equal increase of the osmotic pressure. It seems, therefore, justifiable to assume that the increase in the osmotic pressure or the loss of water on the part of the egg is the cause of the parthenogenetic development of these eggs.

KCl or perhaps the K-ions seem to possess a specific effect upon the eggs of *Chætopterus*, inasmuch as the unfertilized eggs of *Chætopterus* cannot develop into a trochophore if left in normal sea-water, while a small number of K-ions is able to cause them to develop parthenogenetically.

In considering the bearing of artificial parthenogenesis on the theory of fertilization and of life phenomena in general, Loeb says :

The general opinion concerning the rôle of the spermatozoön in the process of fertilization is that it acts as a stimulus, and that as such it starts the development of the eggs. This statement is certainly wrong for those eggs in which we have been able to produce artificial parthenogenesis ; for these eggs, like many others, begin to segment without any spermatozoön if they are left long enough in normal sea-water. The only difference between these and the fertilized eggs is that the former begin to segment much later, and their development stops in the early segmentation stages (2 to 16 cells at the most). The latter may be due to the fact that the egg dies before it has time to develop further.

If we consider the fact that the eggs show at least a beginning of a segmentation under "normal" conditions, the act of fertilization assumes a different aspect. The spermatozoön can no longer be considered the cause or the stimulus for the process of development, but merely an agency which accelerates a process that is able to start with-

out it, only much more slowly. Substances that accelerate chemical or physical processes which would occur without them are called catalyzers (Ostwald). According to this definition we may assume that the spermatozoön carries a catalytic substance into the egg, which accelerates the process that would start anyhow, but much more slowly.

Through these facts and conceptions the phenomena of artificial parthenogenesis assume a different aspect. It would be wrong to say that the K-ions are the stimulus that causes the developmental process. They merely act as catalyzers, accelerating a process that would otherwise proceed too slowly. The loss of water on the part of the egg cell must have a similar effect, but possibly a less direct one. It may be that the loss of water alters the chemical processes in the egg in such a way as to give rise to the formation of a substance which acts catalytically.

Whether or not the catalytic substances introduced by the spermatozoön are identical with those employed in his experiments he cannot say. He considers it probable that in the case of *Chaetopterus* the natural fertilization is not brought about by K-ions, inasmuch as the normal development does not show the characteristics of a treatment of the eggs with K.

Some Ways of Causing Mitotic Division in Unfertilized *Arbacia* Eggs. In 1899 Mathews suggested that blood-clotting and karyokinesis had apparently many points of similarity, and that the processes were possibly identical. In 1900 Loeb suggested that it was probably a liquefaction of certain elements in the egg, possibly of the nuclear membrane, that directly or indirectly produces cell division. Taking up the subject again, Mathews¹ is inclined to agree with Loeb. He found that karyokinetic nuclear division, followed by cell division, could be produced in the unfertilized eggs of the *Arbacia* by methods that ordinarily cause liquefaction in protoplasm, namely, by lack of oxygen, by heat, by exposure to ether, alcohol, and chloroform. Among these the hydroxyl-ion is the most powerful in the production of liquefaction. This is followed by the hydrogen-ion, by lack of oxygen, by strychnine, quinine, pilocarpine, and similar poisons, by loss of water from the cell, replacement of calcium or other ions by potassium, by ether, chloroform, and alcohol, and by a slight increase in temperature.

Further Evidence of the Poisonous Effects of a Pure NaCl Solution. Loeb, having found that the fundulus of a marine fish could not live in a pure NaCl solution of the same concentration as sea-water, Anne Moore,² at his suggestion, repeated his experiments on fresh water

¹ American Journal of Physiology, 1900, vol. iv. p. 343.

² Ibid., p. 286.

fish in order to determine whether the poisonous qualities of a pure NaCl solution is of a general character. Her work tended toward the solution of two problems, namely, Is Na a poison? Does Ca counteract its ill effects? To both of these she obtained an affirmative answer—results in perfect accord with those of Loeb. In addition to these results she found that salts were not directly necessary for the life of young trout or tadpoles, since they may live indefinitely in distilled water, while when salts are present the metal ions Na and Ca must exist in balanced proportions.

METABOLISM.

Physiological and Toxicological Effects of Tellurium Compounds, with a Special Study of Their Influence on Nutrition. In relation to the physiological and toxicological effects of tellurium compounds, Mead and Gies¹ found the following: Non-toxic doses of tellurium (in the forms of oxide, tellurite, tartrate, and tellurate) did not materially affect metabolism in dogs brought to a state of nitrogenous equilibrium, even when dosage was continued for a week. These substances appeared to stimulate proteid catabolism only slightly. They increased somewhat the weight of dry matter in the feces, and diminished in small degree the absorption of fat. The urine was unaffected in volume, specific gravity, and reaction, but became dark brown in color during the dosage periods.

Large doses retarded gastric digestion, induced violent vomiting, loss of appetite, and somnolence. They caused, besides, inflammation and disintegration of the mucous membrane of the gastro-intestinal tract, and also intestinal hemorrhage.

Introduced under the skin, tellurium (tartrate) caused restlessness, tremor, weakening of the reflexes, somnolence, diarrhoea, paralysis, unconsciousness, stoppage of respiration, and death in convulsions from asphyxia. At the point of injection much of the tellurium was deposited in metallic form, but it was also distributed in large quantity to most of the organs and tissues.

Methyl telluride invariably appeared in the breath a few minutes after introduction into the system of even very small quantities of tellurium. It persisted for months after the last dosage. The odor of this substance was also detected in the feces and urine, about the viscera, and in the epidermal excretions.

Secretion of mucus in the stomach and intestines was greatly stimulated by tellurium. Regurgitation of bile into the stomach was a

¹ American Journal of Physiology, 1901, vol. v. p. 104.

frequent result. Tellurium compounds even in small proportion markedly arrested the secretion of acid in the gastric juice.

In the gastro-intestinal tract tellurium compounds were quickly reduced, and the metal deposited in great part in and on the mucous membrane. Intestinal putrefaction did not appear to be influenced in any degree. The intestinal contents were pigmented by reduced tellurium, and much of the ingested substance was eliminated in metallic form in the feces. The action of pepsin and trypsin outside of the body was not very perceptibly diminished by quantities of tellurium compounds under 0.6 per cent. Zymolysis was almost unaffected in the presence of as much as 1.25 per cent. of some of the salts. Ptyalin was more easily affected, even by the faintly alkaline tellurate. Trypsin appeared to be least sensitive to destructive influence, acting rapidly in the presence of even 2.5 per cent. of tellurite.

Tellurium was eliminated in metallic form in the feces; as methyl telluride in the breath, urine, feces, and epidermal excretions; in a soluble form in small quantity in the urine and bile.

The urine was colored brown to yellowish-green after heavy dosage with tellurium compounds, but return to normal coloration was rapid after administration had been discontinued. Albumin and bile pigment, besides tellurium, were the abnormal constituents of the urine found after subcutaneous injections. Toxic quantities given by the mouth caused the appearance of coagulable proteid, but neither bile pigment nor sugar in the urine.

In man tellurous oxide taken into the lungs in fairly large quantity caused nausea, metallic taste, somnolence, depression, and constipation. Methyl telluride was excreted in the breath, through the skin, and with the feces. Inhalations of methyl telluride induced sleepiness and nausea, and the breath and the excretions from the skin under these circumstances acquired and retained for a long time the odor of that substance.

In many respects the action of tellurium in the body is like that of selenium, arsenic, and antimony.

Experimental Poisoning by Acids. Since Walter's experiments it has been supposed that animals that had been killed by acids (1 gramme hydrochloric acid pro kilo of body-weight) had died in consequence of the decrease of the alkalinity of the blood, which had produced, first, an irritation, and, secondly, a paralysis of the respiratory centre. A. Loewy and E. Munzer¹ have repeated the experiments on rabbits with hydrochloric acid and phosphorus, and have come to the conclusion that poisonous doses cause but a moderate

¹ Englemann's Archiv f. Physiologie, 1901, S. 81.

decrease in the alkalinity of the blood; but a considerable diminution in the amount of CO_2 , with a diminished capacity of the blood to take up and find CO_2 . These changes are, however, not of such a decided nature as to furnish a satisfactory explanation for the death of the animal. For this a deleterious influence upon the tissue cells must be held responsible. This would explain the fact that a number of bodies, like phosphorus, iron, arsenic, etc., the poisonous effects of which in the rabbit had been reduced to the effect of acids, are also poisonous to the dog, although this animal by a known mechanism of regulation (Sal-kowski, Walter) is very resistant to the action of acids.

The Nature of Body Sugar. Contrary to the opinion more or less in vogue up to the present time, that dextrose constitutes the only form of sugar existing in the blood, Pavy and Siau,¹ in a series of experiments on horses' blood, confirm a later view. With other recent writers they contend that it is not correct to speak of the sugar of the blood as consisting only of dextrose. In reality it stands in accord with that found in normal urine and muscle. All stand upon the same footing in yielding evidence of the presence of dextrose and of another sugar which gives an ozone that is soluble in hot water and has a crystalline form quite distinct from that of glucosazone and a much lower melting-point, namely, about 153.5°C .

By Baisch and Lemaire this other sugar has been regarded as identical with Fischer's iso-maltose.

Whatever may be the precise nature of the body to which the term "iso-maltose" has been given, it is evident that it is something distinct from glucose. It, therefore, follows from the results that have been obtained that glucose is not the only sugar found in the blood. The same applies to urine and muscle, and inferentially, probably, also, to the other structures of the body.

Fattening with Albumin and Muscle Work. Dr. Karl Bornstein² confirms, from experiments made on his own person, his former conclusions on this subject:

1. An increase in the amount of albumin in the organism, readily accomplished within certain limits by a greater consumption of albumin
2. This albuminous increase ought to be sought for wherever it is desirable to render a cachectic body stronger and healthier.
3. The regeneration of the diseased and weakened cell proceeds much more rapidly with increased albuminous metabolism.
4. Fattening cures are to look, first of all, to an increase in the amount of albumin. The natural albuminous preparations, especially

¹ Journal of Physiology, 1900, vol. xxvi. p. 282

² Archiv f. die ges. Physiologie, Band lxxxiii. S. 540.

the casein sodium (nutrose of Röhmann), are excellent and necessary additions.

The Significance of the Different Food Principles as Generators of Muscular Energy. Prof. N. Zuntz¹ confirms the conclusions of his pupils that fat and carbohydrate may be substituted for each other, as far as work is concerned, in proportion to their heat-liberating capacity through combustion, and that fat need not be changed into a carbohydrate in order to be a source of energy for the muscle. He also confirms the view that the performance of work primarily determines the amount of the metabolism in the animal body.

Fattening by Fat and the Respiratory Quotient. Max Bleibtreu² concludes from his experiments that in the fattening of adult lean geese with superabundant food rich in carbohydrates the respiratory quotient $\frac{\text{CO}_2}{\text{O}}$ in these animals may be pushed considerably beyond unity. The

high values of the quotient are caused by the increase of the excreted carbon dioxide, not by a decrease in the oxygen consumed. The growth of the respiratory quotient beyond the measure possible by the burning of the body substances (unity) proves that the change of carbohydrate to fat in the animal body is connected with a cleavage of carbon dioxide.

The Elementary Composition and the Inverting Power of Glycogen. Dr. Joseph Nerking³ believes, from the analysis of Kekule, that the true formula for glycogen is $(\text{C}_6\text{H}_{10}\text{O}_5)_n$. He finds that the most favorable conditions for the inversion of glycogen consist in the use of a 2 to 2.2 per cent. hydrochloric acid and a boiling time of from three to five hours. According to Sohlet, Lintner, and Düll, about 95 per cent. of starch under the conditions just mentioned may be inverted, and the same proportion, according to Nerking, may be reached in the inversion of pure glycogen.

The Bone-marrow as a Place of Formation of Leucocytes. Werigo and Jegunow⁴ have made a series of experiments to determine what influence, if any, the bone-marrow exerted in the production of leucocytes. They finally came to the following conclusions:

1. The intravenous injection of bacteria stimulates the bone-marrow to increased activity.

2. This activity shows itself by the fact that the bone-marrow now puts forth into the blood a great number of leucocytes.

3. This increase in the output of leucocytes by the bone-marrow takes place according to certain laws, which are quite different for the multinuclear and for the mononuclear leucocytes.

¹ Archiv f. die ges. Physiologie, Band lxxxiii. S. 557.

² Ibid., Band lxxxv. S. 320.

³ Ibid., Band lxxxv. S. 345.

⁴ Ibid., Band lxxxiv. S. 451.

4 and 5. The output of the multinuclear leucocytes does not begin immediately after the injection, but only after a certain time, which varies according to the individuality of the animal (from twenty minutes up to an hour after the injection). It soon reaches a maximum of from twenty to fifty times the number of leucocytes in the arteries, and then begins to decline.

6. The phenomenon is much less marked for the mononuclear leucocytes.

The conclusions just given also hold true when, instead of injecting the whole culture of the bacteria, only the toxins are injected. Mechanical irritation of the bone—*e. g.*, sawing—also stimulates the bone-marrow in a similar way.

DIGESTION. ABSORPTION.

Observations on the Lymph Flow from the Submaxillary Gland of a Dog. Bainbridge¹ summarizes his conclusions, which are confirmatory of those of Cohnheim, Oscher, and Barbera, as follows:

Stimulation of the chorda tympani, stimulation of the cervical sympathetic, and the injection of pilocarpine, all lead to an increase flow of lymph from the salivary gland (submaxillary).

After giving atropine, chorda stimulation no longer causes any increased flow of lymph. The effect of atropine upon the lymph flow produced by cervical sympathetic stimulation is not clear.

Whenever the irritability of the gland is lowered, as after obstructing Wharton's duct, less lymph is obtained by stimulating the chorda than when the gland is normal. The injection of a large quantity of dilute salt solution or clamping the submaxillary vein leads to an increased flow of lymph both before and after the injection of atropine.

On the Changes in Volume of the Submaxillary Gland during Activity. In determining the circulation in the vessels of the submaxillary gland the ordinary method has been to collect the blood escaping directly from one of the gland veins or from the lower division of the jugular vein after tying all the branches opening into it except the veins from the submaxillary gland. On account of the unavoidable hemorrhage by these methods, which go to render the experiment inaccurate, Bunch² chose a method by means of the plethysmograph, which recorded graphically the vasomotor changes of the gland, vessels, and the changes in volume of the gland during activity, which did not involve any hemorrhage during the course of the experiment. By this

¹ Journal of Physiology, 1900, vol. xxvi. p. 79.

² Ibid., p. 1.

method he determined that changes in the volume of the gland may be brought about both by variations in the flow of blood through the gland and of secretion from the gland.

The Theory of the Digestion of Albumin. W. W. Sawjalow¹ considers this question. What is the physiological meaning of the fact that during digestion albumin is first peptonized and then reconstructed from peptones before it enters the blood? He believes that on account of the different constitution of the different albuminous bodies it is necessary that they be converted into a new body which has always the same properties, in order that the blood may maintain the same composition. For this purpose a cleavage of the different albumins must occur—that is, undergo peptonization. By this process all the albumins of the food are decomposed into a series of identical products out of which is formed a new albumin with a constant composition. He therefore finds the physiological meaning of proteolysis not in the removal of the physical difficulty—the absorption of colloids—but in the formation of chemical conditions which may, if possible, form one and the same albumin molecule out of the heterogeneous store of the food, and which thus ensures a constant composition to the blood and tissues independently of the food. The physical changes of the albuminous bodies in the digestive tract he regards only as a secondary phenomenon of the chemical process—only as the external expression of the chemical changes taking place at the same time.

The Present Condition of the Theory of Digestion and Absorption of Fats. Prof. E. F. W. Pflüger² criticises the theory of I. Munk as to the digestion and absorption of fat, according to which fat is absorbed in the form of an emulsion, and presents his own views in the following summary :

1. If the living epithelial cell is examined under the microscope while the fat enters from the intestinal canal there is never seen the smallest drop or granule of fat in the thick cell membrane through which fat must pass. This membrane is as clear as glass.

2. There is an absorption from the intestine even if no fatty emulsion be present.

3. All kinds of fat which permit of a final judgment in this relation are never absorbed in the form of an emulsion, according to the unanimous judgment of all investigators, although they form excellent emulsions and in the intestines are in a fluid state. In order to be absorbed they must suffer a change, during which they are decomposed into fatty acid and the special alcohol.

4. It has been definitely settled that those fats which are glyceryl-

¹ Archiv f. die ges. Physiologie, Band lxxxv. S. 171.

² Ibid., Band lxxxii. S. 303.

esters undergo a very comprehensive cleavage into fatty acid and alcohol. There is, further, no reason to doubt that the separating forces are sufficient to decompose all the fat before its absorption into fatty acid and glycerin. It is also perfectly well known in what way the cleavage products of the glyceryl-esters may be changed into water-soluble bodies capable of absorption.

5. If the fat were absorbed in the form of an emulsion it would form an exception to a very general law, to which, in Pflüger's judgment, it must conform. This law is: Every nutriment, be it albumin, fat, or carbohydrate, is changed in the digestive organs by hydrolytic cleavage into bodies which are soluble in the watery juices of the stomach and intestine in order to be absorbed.

The Movements and the Innervation of the Large and Small Intestine. Some years ago Langley and Anderson made a very accurate investigation of the activity and innervation of the large intestine. Bayliss and Starling¹ have endeavored to find in how far the local reflexes present in the small intestine played a part also in the normal life of the large intestine.

They summarize their conclusions, which apply both to the dog and the rabbit, as follows:

The movements of the large intestine, like those of the small intestine, are under the control of a local nerve mechanism. The peristaltic contraction in the isolated gut is due to a combination of ascending excitatory and descending inhibitory impulses started in the local nerve plexuses by the pressure of a stimulating agent in the lumen of the gut.

The activity of the local mechanism diminishes from the ileocaecal valve to the anus, so that under normal circumstances the extrinsic innervation is of more importance than the intrinsic in the emptying of the lower segment of the colon—*e. g.*, in defecation.

The sympathetic supply to the colon (colonic splanchnics) have a purely inhibitory effect on both muscular coats of the bowel. The pelvic visceral nerve is motor to both coats.

A second investigation on the small intestine² was for the purpose of extending previous observations made on the dog to other animals. They found the general laws applicable also to the cat and the rabbit.

The Influence of Digestion on Animal Heat Processes. Reichert³ investigated in ten six-hour experiments on dogs the influence of digestion on animal-heat processes during the first four hours after feeding, when the mean digestive activity in the dog is probably at its maximum. The animals fasted at least eighteen hours before the beginning of the

¹ Journal of Physiology, 1900, vol. xxvi. p. 107.

² Ibid., p. 125.

³ American Journal of Physiology, 1900, vol. iv. p. 379.

experiments, and were studied for two consecutive hours in the calorimeter before feeding, and for four consecutive hours (with one exception for three hours) subsequent thereto. In three experiments the diet consisted of flesh; in four, of suet; in one, of beef fat, and in two, of flesh and fat. His results are summarized as follows:

1. That the rise of temperature observed during the period of digestion is due to an increase in heat-production.

2. That the temperature gradually rises and reaches a maximum during the fourth hour, or possibly later.

3. That the greatest increase of heat-production occurs during the first hour after feeding.

4. That the changes in temperature and heat-production are not proportional.

5. That the most marked effects, as a whole, are observed when the diet consists of proteid and fat, next with proteid, and least with fat.

6. That the increase of heat-production is not nearly so great as is indicated by the results of the oxygen experiments of Fredericq.

Experimental Researches as to the Place of Resorption in the Liver. Dr. K. Burker¹ concludes from a number of experiments that Heidenhain's theory of interlobular resorption cannot be correct, but that resorption takes place within the liver lobules and especially toward their periphery. He demonstrates the active participation of the lymphatic vessels in the act of resorption by injecting milk into the ductus communis choledochus, when in a short time the lymphatics coming out of the *porta hepatis*, as well as those coming from the perihepatic lymph-glands, take on an intensely white color. The flow of bile varies in pretty regular intervals of from twenty to thirty minutes. The secretion of bile decreases much more rapidly in fasting than in feeding animals. The normal pressure in the great bile-ducts is not more than 75 to 80 mm. of bile. Heidenhain's assertion that the pressure of bile always considerably exceeds the pressure of the blood in the portal vein is not correct for normal relations. The pathological pressure in the great bile-ducts—that is, the pressure which the bile undergoes during an obstruction to the outflow—reaches the value of about 200 mm. of bile, measured in a tube connected with the ductus choledochus. On sudden total closure the pressure reaches smaller values. The pathological bile pressure varies in periods, which are smaller than those observed during the free outflow of bile. After temporary closure of the ductus choledochus the secretory activity of the liver is reduced. Total closure of the duct gives rise to necrotic foci in the periphery of the lobules which has been injured by the bile.

¹ Archiv f. die ges. Physiologie, Band lxxxiii. S. 241.

Here the bile capillaries are ruptured, the bile extravasated, with consequent injury to the liver parenchyma. In this region also the secretion current from the centre of the lobule meets the pent-up bile.

THE CIRCULATORY APPARATUS.

On Reflex Cardiac Inhibition. It has long been known that slowing or arrest of the heart can be brought about reflexly by excitation of almost any afferent nerve of the body if the stimulus be sufficiently great, and that the one nerve which can most readily produce this reflex effect is the vagus. The systematic examination of the different branches of the vagus, with the direct object in view of determining which fibres play the most important part in producing the reflex has not, however, been carried out. Hence, Brodie and Russell¹ designed a series of experiments to show this.

Of the branches of the vagus, excitation of the central end of which causes reflex inhibition of the heart, the pulmonary fibres are those which produce the most marked reaction. The cardiac are much less effective, and the branches below the pulmonary are still less effective.

The connection of the respiratory tract with the cardio-inhibitory centre is very close. Thus stimulation of the nasal mucous membrane is only a little less effective. Stimulation of the trachea and the large bronchi, however, is apparently without effect, but stimulation of the alveolar nerves is about as effective as stimulation of the laryngeal nerves. These nerves produce the result when excited electrically in their course from the mucous membrane or when stimulated mechanically or chemically in the mucous membrane itself.

In addition to the effect upon the cardiac centre, excitation of the pulmonary nerves also acts upon the respiratory and vasomotor centres, producing arrest of respiration and a fall in blood-pressure.

The alveolar nerves can be excited chemically by the inhalation through a tracheal tube of irritant vapors, such as chloroform, hydrochloric acid, ammonia, formaldehyde, or bromine, or by the injection of serum and egg-white.

Division of the pulmonary nerves on both sides completely abolishes the effect upon the cardiac respiratory and vasomotor centres.

Reflex Death of the Heart in Men and Animals. Dr. H. Friedenthal² concludes that the cardiac death in man from psychic influences is caused by a concurrence of vagus irritation, accelerans irritation, want of oxygen, and increase of arterial pressure. All of these factors must

¹ Journal of Physiology, 1900, vol. xxvi. p. 92.

² Archiv f. Physiologie, 1901, S. 31.

enter into simultaneous activity if the nerve centres in the medulla oblongata are stimulated simultaneously, whether the irritation be caused by excessive excitation of the cerebral cortex (fright) or by a surcharge of the nerve centres with carbon dioxide. By stimulating simultaneously both vagi with strong tetanizing currents, Friedenthal could not produce a lasting cessation of the heart-beat, and shows from his experiments that the final cause for the rhythmic movements of the heart must be looked for in the heart itself, and not, as Cyon thinks, in the central nervous system.

The Experimental Analysis of the Irregularities of the Cardiac Impulse. Dr. H. E. Hering, of Prague,¹ has studied the results which follow an increase in the vascular resistance in both dogs and rabbits, and comes to the following conclusions :

1. On increasing the resistance for the emptying of the left or right ventricle irregularities occur in the pulse which are known as the pulsus bigeminus and trigeminus. During the existence of these there takes place a change in the normal succession of the auricular and ventricular contractions, as shown by the fact that the interval between the systole of the auricle and that of the ventricle may become smaller, zero, or even negative, so that a complete reversal of the succession may occur.

2. This change in the normal succession of the auricle and ventricles has its cause in the occurrence of premature ventricular contractions.

3. The prematurity of the ventricular contraction is caused by the circumstance that the ventricles are not excited in the normal way from the auricles. Before the arrival of the stimulus from the auricles the ventricle is made to contract by an abnormal stimulus that acts directly on the ventricle itself.

4. This abnormal stimulus is a mechanical one, caused by the abnormal resistance to the emptying of the ventricle.

5. This mechanical stimulus may even excite the auricle if the normal stimulus proceeding from the large veins does not previously do so.

6. The explanation of the pulsus bigeminus lies in the fact that by premature abnormal stimuli extra systoles are aroused.

7. A pulsus bigeminus may also be caused by extracardial mechanical irritation or by electric stimulation not only of the ventricle but also of the auricle and *venæ cavæ*.

8. While on stimulation of the ventricle the time-value of the bigeminus is equal to the time-value of two regular cardiac beats, such is not the case on stimulation of the *venæ cavæ* and on stimulation of the auricles, except under certain conditions. It is therefore possible up to a certain point to determine from the time-value of a pulsus bigem-

¹ Archiv f. die ges. Physiologie, Band lxxxii. S. 1.

inus which part of the heart was first excited by the pathological cause.

9. These irregularities are of a myogenic nature, like the entire normal activity of the heart. A bigeminus of neurogenic origin is unknown.

10. A hemisystole or systolia alterans, in the clinical sense, cannot be demonstrated on the hearts of animals. The reports of observations of such hemisystoles depend upon illusions caused by defects of the registering apparatus.

The Rhythmic Activity of the Heart Muscle during the Passage of Constant Currents. Since Eckhardt's observations it has been known that the cardiac apex which is free of ganglia is capable of executing a series of rhythmic contractions during the passage of a constant current, if of sufficient intensity. Kaiser explained this phenomenon by assuming that the current was only apparently constant. Trendelenburg,¹ in the present essay, shows that a perfectly constant current is capable of causing rhythmic contractions of the cardiac apex. As Langendorff has shown that the same results follow constant stimulation by chemical means, the general correctness of the view must be admitted, and every theory of cardiac activity will have to regard this property of the cardiac tissue as an important factor.

The Effect of Maximum Muscular Effort on Blood-pressure. McCurdy² affirms that the teaching of gymnastics can scarcely be said to rest upon a sound basis of physiological knowledge, since not even the effect of exercise on blood-pressure has been determined with precision. He therefore investigated the blood-pressure during "exercises of strength or effort." It was considered best to select one clearly defined typical exercise of strength rather than attempt the study of blood-pressure in a variety of movements. The exercise selected was a combination of the back and leg lift used in the physical examination of most college students. The subject stood with bent knees, with the left hand he grasped the middle of the handle of the dynamometer, either end of which rested on the front of the thigh. At the word he extended his legs and straightened his back with all his strength. From three to five lifts were necessary to determine the highest blood-pressure. The pressure was recorded in sixty-seven experiments on twenty-three men before, during, and two or three minutes after the maximum lift. The average of all the movements was as follows :

	Subject standing.	Subject lying.
Blood-pressure in mm. of mercury before lift . . .	111	110
Blood-pressure in mm. of mercury during lift . . .	180	
Blood-pressure in mm. of mercury two and three minutes after lift	110	110

¹ Archiv f. die ges. Physiologie, Band lxxxii. S. 268.

² American Journal of Physiology, vol. v. p. 92.

It appears, therefore, that the blood-pressure undergoes a sudden and great increase during the lift, and that it falls very rapidly to normal as soon as the muscular effort ceases. This rise in pressure is not accompanied by any great change in the pulse-rate. In seventeen examinations on nine individuals during the five seconds of the lift and the fifteen seconds immediately following, seven showed an average increase of five beats per minute; seven showed a decrease of four beats, and three continued at the same rate. The pulse-rate in these cases returned to normal one minute after the lift.

Observations on the Changes of Blood-pressure during Normal Sleep. An interesting study of the changes in blood-pressure during normal sleep was made by Brush and Fayerweather.¹ The observations were made throughout the whole period of sleep from night until morning. They determined that during sleep the blood-pressure falls during the first few hours, and then gradually rises up to the time of awaking. This rise is not regular, but is broken by long waves, although the general tendency of the pressure is toward a steady increase. On waking in the morning the arterial pressure is greater than just before sleep at night, when the pressure is measured in the same (reclining) position. With reference to the theories of sleep, these observations show that the rise of pressure on awaking is not sudden, but is the culmination of an increase that begins to appear within an hour or two after sleep is begun. This fact would seem to indicate a progressive vasoconstriction during most of the period of sleep, and to this extent it is in harmony with the so-called vasomotor theories of sleep.

The Physiological Action of Three Poisonous Toadstools—*Amanita Muscaria*, *Amanita Verna* or *Bulbosa*, and *Amanita Phalloides*. Dr. W. S. Carter² undertook the investigation of the three poisonous mushrooms or toadstools which most frequently cause death in man, namely, the *A. muscaria* or "fly" mushroom, the *A. verna*, and the *A. phalloides* or "death-cup."

He found in all three that the most prominent action was on the circulation.

AMANITA MUSCARIA. In this the principal effect consisted in inhibition of the heart, with a great fall of blood-pressure. This was prevented or removed by injections of atropine, but not by cutting of the vagi. The action, therefore, must have been upon the inhibitory mechanism within the heart; the fact, also, that some vasodilatation is produced which contributes to the fall of blood-pressure, though this is less prominent than the cardiac inhibition. When the circulation was seriously altered the respirations were generally slow and shallow.

¹ American Journal of Physiology, vol. v. p. 199.

² Ibid., p. 158.

Vomiting and purging occasionally took place late in this poisoning, but much less frequently than with the other two. Convulsions were never observed. Usually coma appeared late in the poisoning, but in a few instances it began early and persisted until death. There seemed to be no difference in the physiological action or in the susceptibility of different animals (dogs, cats, rabbits, and frogs). Atropine is of undoubted antidotal value.

AMANITA VERNA. Inhibition of the heart was less pronounced and less persistent. There was slight inhibition when the vagi were cut previous to administration, but never so great as when the vagi were intact. Section of the vagi after cardiac inhibition has been produced by the poison does not entirely do away with the inhibition. Atropine, however, causes it to disappear. It would seem, therefore, that *amanita verna* acts both upon the cardio-inhibitory centres in the medulla and upon the inhibitory mechanism within the heart. Its chief action, however, seems to be upon the vasomotor mechanism, causing a widening of the vessels. Respirations were usually slow and frequently irregular. Convulsions were frequently observed. Atropine appeared to be of very little value as an antidote, although the experiments were not sufficiently numerous to warrant a positive conclusion.

AMANITA PHALLOIDES. The action of *amanita phalloides* upon the circulation is very similar to that of *amanita verna*. There is some inhibition of the heart, but it does not occur constantly, neither is it so pronounced or so lasting as in poisoning by *amanita muscaria*. Previous section of the vagi prevents this inhibition of the heart. This indicates that the chief action is upon the inhibitory centre in the medulla. Independently of the cardiac inhibition there was also a great fall of blood-pressure, apparently due to vasodilatation caused by paralysis of the vasomotor centres. The respirations were slower than normal and at times irregular. Usually coma came on late in the poisoning, though when the poison was given rapidly or in large quantities it came on early and persisted until death. Convulsions did not occur. Atropine is of little service as an antidote, since it causes only the inhibition of the heart to disappear, which is not an important factor. Boiling or drying or the extraction of the toadstools by alcohol or water produces no difference in toxicity. After fatal doses no structural changes of the neurons could be found.

The Immediate Action of an Intravenous Injection of Blood-serum. In carrying out some experiments with antitoxic serum, Brodie¹ found to his surprise that the intravenous injection of diluted blood-serum into a cat produced a marked effect upon the heart and

¹ Journal of Physiology, 1900, vol. xxvi. p. 48.

respiration. On account of the extensive employment of serum in therapeutics he undertook to follow out his observation. Dogs, rabbits, and cats were experimented on, but the effect was observed only in the cat. Moreover, the effect was produced not by the injection of anti-toxic serum alone, but serum from any source, including even the serum obtained from another cat. It was also found that several other substances—*e. g.*, egg-white and the bromine compounds of proteids—could produce the same effect, though in his experiments serum was chiefly employed. Finally, milk had a slight effect, though gelatin and peptone none. This subject is not new, such effects having been described previously by Weiss, Guinard, Dumarest, Friedenthal, and others.

A summary of his experiments showed that intravenous injections of blood-serum from any source into the cat causes arrest of respiration, inhibition of the heart, and vasomotor dilatation, which persists for some time. These effects are reflex, and are due to the excitation of the pulmonary nerves. They are not affected by division of the cardiac or lower branches of the vagus, though are absent on division of the pulmonary branches or of the vagus itself in the neck. Repeated injections produce immunization, the reaction on respiration usually disappearing first; on the heart and bloodvessels later. The active substance in the serum was found to be a proteid of the albumin class coagulable at 86° C., and is produced only when the blood clots. Moreover, the interaction of the blood-corpuscles was proven necessary for its formation. Serum obtained from plasma was inactive.

The Relation of the Depressor Nerve to the Vasomotor Centre. Porter and Beyer¹ affirm, from a series of carefully controlled experiments on rabbits, that there is not sufficient evidence that the depressor nerve forms a special connection with the cells which control the vasomotor fibres of the splanchnic nerves. It is probable that the depressor nerves connect in the same way with all the cells in the bulbar vasomotor centre, and there is no reason to suppose that other afferent vasomotor nerves differ in this respect from the depressor nerve. Afferent vasomotor fibres would thus influence all the bulbar vasomotor cells alike, and the bulbar centre would have no part in the distribution of the blood to the several organs and regions of the body. The bulbar centre would act merely to raise or lower the general blood-pressure.

GLANDS.

The Composition and Action of Orchitic Extracts. In a rather careful investigation Dixon² found that the fresh testis macerated with

¹ American Journal of Physiology, 1900, vol. iv. p. 283.

² Journal of Physiology, vol. xxvi. p. 244.

physiological salt solution contained three groups of bodies: (1) A proteid; (2) organic substances unaltered by boiling; and (3) inorganic salts. He found in cats, dogs, goats, and rabbits of either sex that extracts of the testes of almost any animal produced physiological effects which differed somewhat in different animals. In the cat, for instance, there is a double fall of blood-pressure. The first, immediate, though slight, and followed by quick recovery; a second, thirty to fifty seconds later, associated with cardiac inhibition, from which recovery is gradual, yet complete in a few minutes. In the dog only the first fall of pressure is noticed. The rabbit is extremely susceptible, and shows a double fall. The goat, on the contrary, shows an initial rise of blood-pressure, followed by a drop to normal, and forty seconds later a second more considerable rise. Disturbances of respiration are also seen. Both these and the cardiac effects are absent if the vagi have previously been severed, so that they would seem to be of central origin. The extract likewise produces a prolonged hypoleucocytosis, followed by a hyperleucocytosis. This hypoleucocytosis is largely the result of an altered distribution of the leucocytes, and mainly affects the polynuclear variety. All these effects are practically due to the nucleoproteid contained in the extract.

The effect of the second group of bodies may be observed after either the administration of the filtrate from the boiled extract or the administration of the gland by the stomach when the nucleo-proteid effect on the heart and respiration is eliminated. The action of this group of substances corresponds closely to the action of a number of leucomaines, of which choline may be taken as an example.

Spermine is responsible partially, but probably only in a small degree, for this effect, because an alcoholic extract of testis in which spermine is soluble produces the same effect. Orchitic injections produce similar effects on animals which have been castrated some months previously and on the normal animal.

Diuretic Effects of Sodium Chloride Solutions: An Inquiry into the Relation which Certain Factors Bear to Renal Activity. Considerable literature has been devoted to the different effects which follow the introduction of sodium chloride solution into the circulation. Thompson¹ has taken up this subject again, and emphasizes the following facts which, though noticed previously, were not insisted upon:

In many cases a small intravenous injection of physiological or isotonic solution of sodium chloride brings about a diuresis out of all proportion to the quantity of the solution injected.

The pronounced diuretic effect begins to appear toward the end of

¹ Journal of Physiology, vol. xxv. p. 487.

the first hour after the injection, and reaches its maximum in the first half of the second hour. It then gradually declines throughout the third and fourth hours, at the end of which time the secretion has, as a rule, become normal.

The excretion of nitrogen and of urea is considerably augmented; the increase, however, reaches its maximum in the first hour after the injection, and thus does not coincide with the maximum outflow of urine.

The diuresis is not caused by an elevation of blood-pressure. On the contrary, a fall of pressure often takes place during the hour of greatest secretion of urine. The fall is probably to be attributed, in part, at all events, to the great escape of water through the kidney. It is most marked in experiments where the diuresis is greatest. The commencement of renal activity is accompanied by a hydræmic condition of the blood, which no doubt plays an important rôle in causing the diuresis. It is not, however, the sole factor, since the maximum of the hydræmic state does not correspond with that of the diuretic effect; moreover, the hydræmia has ceased to exist long before the activity of the kidney has returned to normal. Further, a hydræmic condition does not always occasion diuresis.

On the Effects of Venous Obstruction on the Secretion of Urine.

In a recent paper, Schwarz states that ligation of the renal veins always caused extensive clotting in these vessels, and he ascribes the cessation of urinary secretion not to the venous obstruction, but to the clotting, adding that if by a process of preliminary defibrination the dog's blood be rendered non-coagulable the clotting in the renal veins will be prevented, and ligation of these vessels will not produce a diminution but an increase in the secretion of urine. This statement was of such importance in regard to the general theory of urinary secretion that De Souza¹ reinvestigated the whole question while paying particular attention to the repetition of Schwarz's experiments, and, in contradiction to Schwarz, put the subject back on its former basis.

Reflex Anuria. Dr. A. Goetzl² refers to a clinical case in which, in a man, anuria was caused each time by an enormous increase of the intrarenal pressure in intermittent hydronephrosis. Here the great increase of the intrarenal pressure caused by the temporary impermeability of the ureter on the one side stopped the secretion of the kidney on the opposite side by reflex action; for the removal of the intrarenal pressure in the diseased kidney, by puncture, at once removed the inhibition of the secretion of the healthy kidney, for at

¹ Journal of Physiology, vol. xxvi. p. 139.

² Archiv f. die ges. Physiologie, Band lxxxiii. S. 628.

once a polyuria from this organ occurred. The author succeeded in proving by experiments on dogs that a one-sided increase of pressure produces a reflex anuria. He found also that it is not the height of the pressure in the kidney, but rather a certain steadiness of the pressure which is the essential element.

The Physiological Effects of Some Products Obtained from the Thyroid Glands. Cyon and Oswald¹ investigated the physiological effects of (1) the thyreoglobulin of the pig and sheep; (2) the iodothyryn obtained from the thyreoglobulin; (3) the thyreoglobulin of calves free from iodine; (4) an iodine-containing solution obtained from human thyroid glands by tryptic digestion; (5) the iodine-containing residues which are formed during the production of iodothyryn, and from which no more iodothyryn can be extracted; and, finally, (6) the iodic albumoses and peptones which are formed during the digestion of the thyreoglobulin by means of pepsin and hydrochloric acid. They have come to the following conclusions: The first substance, containing 0.06 per cent. of iodine in organic union, produces diminution of blood-pressure and stronger but slower action of the heart, which was not interfered with by section of both vagi. The third substance proved to be inert; the fourth produced a considerable increase of blood-pressure, with acceleration of the heart-beats, while the fifth and the sixth products were found to be without any influence on blood-pressure and pulse. From these experiments the authors infer that the thyreoglobulin must be regarded as the albuminous substance which contains the iodothyryn complex in its molecule, and that the remaining products obtained from the thyroid gland do not possess the physiological properties of the iodothyryn, though they contain iodine.

On the Effects of Complete Removal of the Suprarenal Glands. Moore and Purinton² completed their series of experiments begun last year. Their experiments were made on fifteen cats and three goats. They found that complete removal in the cat was followed in all cases by a fatal result, the longest period of survival being just under five days. In three of the experiments on the cats extensive ante-mortem clotting in the right heart, superior vena cava, and pulmonary artery was found, and in these the duration of life was shorter than in those in which no such clots were found. The chief symptoms manifested by the cat after complete removal were muscular weakness, followed by extremely rapid, shallow, and irregular respirations and rapid clonic muscular contraction affecting the whole system of the skeletal muscles.

¹ Archiv f. die ges. Physiologie, Band lxxxiii. S. 199.

² American Journal of Physiology, vol. v. p. 182.

Death took place in respiratory failure, the heart continuing to beat for some time after respiration had ceased. The removal of both suprarenals in the goat caused death in only three out of four cases. The average period of survival in the three goats which succumbed was much longer than that in the cats. No clonic contractions were observed in the goat at any period, the chief symptoms being extreme muscular weakness and rapid, shallow respiration.

Studies of the Metabolism of the Dog Before and After Removal of the Spleen. Although various theories have been propounded as to the influence of the spleen in metabolism, no systematic investigation on the subject has been recorded. Realizing this, Noël Paton¹ studied the metabolism before and after the removal of the spleen. His conclusions, though important, are brief, viz.: There is a more rapid excretion of water after a meal, probably indicating a more rapid absorption. There is no essential difference in the course or nature of the metabolism, either during or after feeding with the ordinary proteids of flesh, with vegetable food, such as oatmeal, or with food rich in nucleins, such as thymus.

NERVOUS SYSTEM.

The Effect of Limited Nerve Compression. Dr. V. Ducceschi,² at the Physiological Institute at Rome, has employed a peculiar method of his own, by means of which he could apply pressure to a very limited area of a nerve. He found that if a suitable pressure be applied to a nerve it is possible to momentarily suppress the propagation of the nerve impulse or to diminish the intensity of the impulse. The restitution of function is more or less complete according to the intensity and duration of the pressure. Only rarely is there a short interval of increased function before the suppression of the conduction, provided the compressed area is small in extent. The conduction of the impulse is influenced in the same way by the compression, no matter whether the impulses were generated by mechanical or chemical stimuli. He also found, in agreement with the observations of Lederbaum, that under the influence of weight the conduction ceases first in the sensory and later in the motor nerves.

Nerve Stimulation by Frequent Alternating Currents. W. Einthoven³ disproves the current view that on overstepping a certain frequency in the application of electric stimuli to a motor nerve the contraction will decrease in intensity according as the frequency of the

¹ Journal of Physiology, vol. xxv. p. 443.

² Archiv f. die ges. Physiologie, Band lxxxiii. S. 38.

³ Ibid., Band lxxxii. S. 101.

stimulation increases. From his experiments he concludes that an alternating current of about one million periods per second is still able to stimulate a nerve. The muscle contracts very feebly if the strength of the current just reaches that amount which is necessary to produce a reaction. With the increase of the current the muscle contracts more strongly until the contraction reaches a maximum beyond which an increase in the strength of the current has no further effect. In this regard the frequent alternating current does not differ from the stimulating effect of other electric stimuli, but there is a great difference in the minimum strength of current necessary to produce a contraction. Einthoven found, for example, that while the muscle reacted to a constant current of 0.595 microampère, an alternating current of 8.8×10^5 periods per second had to be 16,250 times as strong to just stimulate the same muscle.

It was formerly believed that the high-frequency Tesla currents did not enter the body at all, and it was on this ground that the experiment of Tesla—lighting an incandescent lamp with the finger—could be explained. Now, Dr. Einthoven appears to have shown the incorrectness of this view, as his experiments prove with great clearness that the Tesla alternating currents of, for example, one-million periods per second may stimulate a nerve. Dr. J. L. Hoorweg¹ shows how his formula for the law of nerve stimulation is able to explain that for each stimulation by alternating currents there is a certain value of frequency to which the nerve is most responsive. He thinks that his law can explain all the observed facts as to the effects of alternating currents.

New Experiments on the Action Current in Nerves that Cannot be Stimulated. From a series of experiments on this subject Radzinkowski² concludes: 1. The action current may develop in the part of a nerve which, on account of treatment with ether, etc., can no longer be stimulated. It arises in consequence of a stimulation of an irritable part, and *vice versa*. 2. The action current may also be observed in nerves which cannot be stimulated at all in any part of their extent. 3. Nerves which have been narcotized by the vapors of ether or chloroform lose their influence upon the muscle long before they lose the capability of developing action currents on faradic stimulation. 4. The restitution of the irritability progresses apparently from periphery to centre. Nerves in which the irritability is again restored in one part are the best in which to observe the facts upon which rests the first conclusion.

The Fundamental Properties of Nerves under the Influence of Some Poisons. The new doctrine, according to which the conductivity

¹ Archiv f. die ges. Physiologie, Band lxxxiii. S. 89.

² Ibid., Band lxxxiv. S. 57.

and the irritability of the nerve are two radically different properties, as has been asserted by Grünhagen, Schiff, Gad, and others, has been re-examined by N. E. Wedensky.¹ He made his experiments with four nerve poisons—cocaine, chloral hydrate, carbolic acid, and chloralose—and comes to the following conclusions :

1. The method hitherto used to determine local changes of conductivity in the narcotized portion of the nerve by the minimal stimuli applied to the non-narcotized portion does not lead to correct conclusions. This method still shows an unchanged conductivity, while in reality the local conductivity suffers an ever-increasing change, which is demonstrated, first, by a constant decrease of the negative variation at the galvanometer and by a peculiar change in the rhythmic character of the tetanizing stimuli (in the telephonic nerve sounds), and then by a rapid decrease in the muscular contractions produced by strong stimuli.

2. Later on strong impulses are arrested by the narcotized portion, or they produce only an initial contraction, while very moderate impulses are still able to pass this portion and to produce tetanic contractions. The conduction of the weakest impulses is the last to be arrested.

3. The irritability of the narcotized portion decreases only gradually, and at the time when this portion becomes completely impenetrable to the impulses conducted from above it still retains a considerable value. That we have to do here with a condition of the nerve rather more complicated than has hitherto been thought is shown by the fact that the reduction of the irritability occurs in a different ratio for the ascending and descending induction currents.

4. The local application of the nerve poisons shows a remarkable and complete parallelism between the changes of the functional properties of the nerve and the changes of the action currents.

5. The assertion recently made that under the action of chloralose there was not such a parallelism is incorrect.

6. The ability of the nerve to recover can be observed also after the effect of weak solutions of cocaine and phenol.

The author is inclined to regard the state of the nerve under the influence of narcotics not as a passive one, but rather as an active one, as a peculiar state of irritation which influences not only the stimuli applied directly to the changed nerve portion, but also the impulses as well.

The Physiology of the Nerve Inhibition Phenomena. Max Verworn² defines inhibition as the phenomenon that occurs not only when an existing muscle contraction is stopped, but also when the occurrence

¹ Archiv f. die ges. Physiologie, Band lxxxii. S. 134.

² Archiv f. Physiologie, 1900, Supplement Band.

of a muscle contraction is prevented or made more difficult by way of the nerves. There are three possibilities which might explain this phenomenon :

1. The motor stimulation of the ganglion cells in the anterior horn, which produces the contraction, is inhibited itself, and in consequence of the cessation of their motor impulses the contraction of the muscle stops by itself.

2. The muscle is provided not only with motor neurons, but also with inhibition neurons, which by their impulses inhibit the contracted muscle—*i. e.*, suppress an existing contraction or hinder the occurrence of a contraction.

3. The motor cells of the anterior horn produce themselves an active inhibition of the muscle by transmitting through their axis-cylinders to the muscle an active process of inhibition which is qualitatively opposed to the motor impulse.

The last theory has been formulated by Starke, the second by Gaskill and others, while the first is that accepted by most physiologists.

Verworn disproves the second and third views by his experiments, which show that the central inhibition of a skeletal muscle has no influence upon the absolute height of the contractions which are produced by direct stimulation of its nerve. The inhibition of the skeletal muscle is only a passive act. There is, however, an active inhibition in those tissues which have their own tonus. This active inhibition offers many difficulties to a physiological analysis. Verworn favors the view that inhibition here is due not to a special process in the inhibitory nerve, but to the specific end organ of this nerve.

Experiments Concerning the Prolonged Inhibition Said to Follow Injury of the Spinal Cord. Porter and Muhburg¹ made a series of long-continued observations on animals in which spinal cells known to take part in some automatic function had been separated from the brain, in order to determine whether the loss of function following the isolation was permanent or temporary. If permanent, the separated cells cannot be automatic in their action, but must depend for their rhythmic discharge on stimuli received from other nerve cells. If the loss of function be only temporary the isolated cells may have been inhibited or may have gradually developed power unused since foetal days. The phrenic cells were selected for the experiments.

The two sets of phrenic nuclei were separated from each other by a median longitudinal section of the spinal cord. At the anterior (cranial) end of this median section the cord was hemisected. The phrenic cells of the one side were thus completely isolated from those of the opposite

¹ American Journal of Physiology, vol. iv. p. 334.

side and from the brain. The animals were kept alive, and after days or weeks the isolated cells were shown to be still functional by making them discharge motor impulses. The diaphragm was exposed and directly inspected to determine whether the half of the muscle innervated through the isolated phrenic cells contracted rhythmically. The animals employed were cats and rabbits.

In every instance the separation of the phrenic cells from the brain caused the permanent arrest of the corresponding half of the diaphragm. This arrest is held to be an excellent example of prolonged inhibition in consequence of injury to the spinal cord, but it is shown in the present investigation that the phrenic cells after their isolation are still able to discharge motor impulses, though their apparent automatic rhythmic respiratory power is gone. This cannot be ascribed to inhibition, therefore, and the collapse of the hypothesis in this conspicuous instance warrants the belief that injuries of the spinal cord do not cause prolonged inhibition.

On the Origin from the Spinal Cord of the Vasodilator Fibres of the Hind Limb, and on the Nature of these Fibres. The experiments of Bayliss¹ seem to practically settle the question definitely insisted upon for the first time by Stricker in 1876, namely, that there are vasodilator fibres in the posterior roots of the fifth, sixth, and seventh lumbar and first sacral nerves, and there is no evidence that the hind limbs receive vasodilator fibres from any other sources.

These fibres do not pass into the abdominal sympathetic chain, and, therefore, must proceed directly into the lumbosacral plexus.

They do not degenerate when cut between spinal cord and posterior root ganglion, hence they are not spinal efferent fibres. They do degenerate when posterior root ganglia are extirpated, hence their "trophic centres" are in these ganglia.

They are, in fact, identical with the ordinary sensory afferent posterior root fibres. The name "antidromic" is suggested for the process by which nerve fibres convey impulses in a direction contrary to that assumed by the Bell-Magendie law, where such impulses produce effects in the organs at the origin of such fibres—*e. g.*, when afferent fibres excited at their ends in the central nervous system produce vascular dilatation at their peripheral ends in the tissues of the body.

The Physiological Significance of the Hippocampus Major. From his experiments on dogs Dr. V. P. Ossipow² concludes that the hippocampus major, contrary to the opinion of Ferrier and Yeo, must not only not be regarded as the centre of the muscle sense and cutaneous

¹ Journal of Physiology, vol. xxvi. p. 173.

² Archiv f. Physiologie, 1900, Supplement Band, S. 1.

sensibility, but that its function has no connection at all with either of these senses.

The relation of the hippocampus major to the senses of sight, hearing, taste, and smell must also be very much doubted, for the reason that after the method of the abolition of the function he did not succeed in showing any observable deviations from the normal in these senses.

Fatigue, Exhaustion, and Recuperation of the Nerve Centres of the Spinal Cord. Max Verworn¹ used the method of strychnine-poisoning in order to investigate the physiological processes in the living substance of the neurons. With regard to strychnine, he had made it probable by former experiments that it *does not* affect the motor neurons of the anterior horns, and, later, Baglioni had shown conclusively that the poison did not affect these motor cells, but only the sensory elements of the spinal cord, and most probably the cells of the posterior horns, which latter are brought by the strychnine to such a high degree of tension that the weakest stimuli readily produce an enormous excitation which is communicated to the motor neurons of the anterior horns, and thus give rise to the violent reflex contractions. This action of the strychnine, Verworn thinks, is the only action it has on the spinal cord, and he believes that the paralyzing effect observed after large poisonous doses must be due to the asphyxia caused by the diastolic cardiac paralysis.

He shows that fatigue may be regarded as a paralysis due to the accumulation of waste matter, and exhaustion as a paralysis due to the want of nutritive material. For the process of recuperation he proves that the removal of the paralyzing products of metabolism alone does not suffice, but that it only takes place in reality after new oxygen has been supplied.

The Effect of Strychnine Upon the Spinal Cord and Peripheral Nerves. Contrary to the views of Verworn, Dr. Biberfeld² finds that the paralyzing action of large doses of strychnine is not due to the asphyxia from cardiac paralysis, but to a direct paralyzing action on the spinal cord itself. As to the nerve end-apparatus, Biberfeld further shows that strychnine paralyzes not only the motor but also the sensory end-apparatus.

Studies on the Influence of Strychnine on the Spinal Cord of Rabbits. Dr. H. A. Hare³ has recently published the results of a series of experiments the objects of which were to determine whether immunity to strychnine may be produced, and to find, if possible, the exact portions of the spinal cord upon which this drug exercises its

¹ Archiv f. Physiologie, 1900, Supplement Band, S. 152.

² Archiv f. die ges. Physiologie, Band lxxxiii. S. 397.

³ American Journal of Physiology, vol. v. p. 333.

chief effect. For this purpose it was necessary to determine, first, the amount of strychnine which, when given to an animal hypodermically, would just give rise to a convulsion. This was termed the convulsive dose. After a number of trials this amount was found to be about 0.00085 to 0.0009 gramme for a rabbit weighing 2000 grammes. This having been settled, the next step was to determine if immunity to larger doses could be established by the administration of gradually increasing, but smaller, doses extending over a given period of time. Three rabbits, weighing on the average 2100 grammes, received for a week increasing doses of strychnine, beginning with 0.00015 gramme and increasing daily by the 0.00005 gramme. None of these doses produced convulsions, but the last dose—0.0006 gramme—produced a decided increase in reflex excitability. Again it was found that animals which had received frequent repetition doses died from convulsions when they received 0.0008 gramme, while animals without previous use of the strychnine did not have convulsions at all. From these and similar experiments Dr. Hare concludes that frequent repetition of the doses rather increases than decreases the susceptibility to the drug, and for this reason physicians who desire to give full doses of this drug may do so at once without fear of producing over-effects.

It was observed in these experiments that the strychnine affected the posterior extremities more promptly than the anterior, and that the exhaustion paralysis of the former was marked, whereas the latter speedily regained their power.

The spinal cord of a number of the animals investigated was examined by Nissl's method by Professor Simon Flexner to discover whether any demonstrable changes had been produced in the spinal cells. The results were, however, practically negative. The majority of the cells showed a perfectly normal form, and arrangement of stichochrome granules. A small number of cells showed slight central chromatolysis with partial migration of the nucleus toward the periphery of the cell. In no instance was the nucleus in immediate contact with the wall of the cell, and the only cells which showed any change whatever were the cells of the anterior horns. The cells of the intervertebral ganglion were normal.

Ergographic Studies in Neuromuscular Fatigue. In an extensive series of experiments Hough¹ worked with a new ergograph, his own modification of Mosso's. The principal modification in it consisted in the use of a spring instead of a weight in the prone instead of the supine position of the hand, in confining the flexion to the second and third phalanges, and in the maintenance of a constant leverage to each

¹ American Journal of Physiology, vol. iv. p. 240.

subject of experiment. Hough, however, admits that the weight of the ergograph has special advantages in certain cases. With his own ergograph the findings were somewhat different to the usual ones; for example, the curve of fatigue in the trained muscle falls as an asymptotic curve to what is practically a constant fatigue level. The height of the fatigue level varies inversely with the rapidity of the rhythm of contraction.

Moreover, he claims that the rhythmic variations in most ergographic tracings are the result of errors of experiment. The more completely these errors are eliminated the less noticeable are the variations.

In the trained muscle the variations in the height of the initial contraction and of the fatigue level may be and possibly always is very slight from day to day. Marked variations, on the other hand, occur in the time required to reach the fatigue level, and his results suggest that there is some relation between this and the time of day the experiment is made.

The phenomena of "second wind" and of "warming up to work" seems to be entirely absent from the work of the simple neuromuscular mechanism.

Smoking failed to produce any effect upon the curve of fatigue except, possibly, to prolong the duration of the fall to the fatigue level. He finally states that the experiments of Mosso and Lombard on alternate electrical and volitional stimulation of muscles do not justify the conclusion that the nerve cell fatigues more rapidly than the muscle fibre.

Changes in the Blood During Exercise. Wetzels,¹ according to the method of Hering, joined one carotid artery to one jugular vein, shutting off all the other arteries and veins except those that belonged to a certain organ. The pulmonary circulation was not interfered with. The organ in question—for example, the leg—was then stimulated by induction currents and the blood examined. It was found after the artificial muscle activity the coagulability was retarded that the number of erythrocytes showed a slight decrease, and that the number of the leucocytes was decidedly decreased. It was observed that the alkalinity of the blood was also reduced.

Experimental Researches on Man as to the Influence of Muscular Work upon the Metabolism and the Importance of the Single Food as a Source of Muscle Energy. The main results of this investigation is the negation of the assertion of Seegen and Chauveau that fat had to undergo a change into carbohydrate before it could be used by the human body for muscular work. Prof. Newton Heinman² shows

¹ Archiv f. die ges. Physiologie, Band lxxxii. S. 505.

² Ibid., Band lxxxiii. S. 441.

from his experiments that fat is the better source of energy for the active muscle, while, according to the hypothesis of Chauveau, we should find a consumption of energy higher by 29 per cent. than when sufficient carbohydrates are at the disposal of the muscle.

The Source of Muscular Energy. Prof. Dr. Frenzel and Dr. F. Reach¹ came to the conclusion from their experiments on each other that fat and carbohydrates by their oxidation in the animal body are able to furnish kinetic energy according to their caloric value in an almost equally economic manner. Regarding the albumin experiments, they do not regard their work as conclusive.

The Action of Ether and Chloroform on the Neurons of Rabbits and Dogs. In order to determine whether chloroform and ether produce transient or permanent changes in the cortical and spinal neurons, Wright² made some very thorough experiments, from which it is only possible to give his conclusions.

In his first paper on this subject he showed that both ether and chloroform produce in dogs and rabbits certain changes in the nerve cells. The Nissl granules lose their affinity for methylene blue, and the cells possess a rarefied, or, in extreme cases, a skeleton-like appearance. By Cox's method the dendrons are found to present moniliform enlargements. These changes, which he attributes to the biochemical action of the anæsthetic on the substance of the nerve-unit, become more pronounced as the anæsthesia is prolonged, and are more readily induced in rabbits than in dogs. The nerve cells of dogs show little or no change until the anæsthesia has been prolonged for more than four hours.

His second paper presents the results of five more experiments on dogs which supplement and extend these observations. The object of these experiments were twofold :

1. To determine whether a still more prolonged period of anæsthesia renders the changes more intense.
2. To ascertain whether the pseudo-degenerative change is permanent, by an examination of the tissues of the animals, after the anæsthesia had passed off.

It may briefly be stated at the outset that the answer to the first question is in the affirmative, and to the second in the negative.

These further observations confirm his previous work and show that ether and chloroform act directly upon the chromatic substance of the perikaryon, chemically changing it so that it loses its affinity for aniline dyes. This biochemical change is more intense in the experiments now recorded than in those previously described, the anæsthesia having been

¹ Archiv f. die ges. Physiologie, Band lxxxiii. S. 477.

² Journal of Physiology, vol. xxvi. 1900, p. 30, and 1901, p. 362.

kept up longer. In these later cases even the nuclei and nucleoli are affected. The nucleolus is the last part of the cell to show the effect of the drug. The slow return of the conjunctival reflex in these cases appears to indicate that after a certain period of anæsthesia (six hours in the dog) the depression of the neuronal function becomes more rapidly profound, and that there is a limit to the time of safe anæsthesia. The histological changes observed support this view, for a greater alteration occurred in the cells during the three hours between the sixth and the ninth of anæsthesia, than during the five hours between the first and sixth hours.

The experiments also show that the changes described in the cells are only transitory. They disappear with the disappearance of the drugs from the blood and tissues or soon after. Certainly after nine hours of ether narcosis the cells are practically normal forty-eight hours later. There is no permanent deformity in the cells, and no degeneration of their processes.

This observation affords further evidence that the moniliform swelling of dendrons is not due to simple retraction of the neurons, but is the result of a pathological change in the trophic centre of the neurons. It is analogous to the swelling observed in the first stage of atrophy in axons when cut off from their trophic centres.

The rarefaction of the cell substance and the formation of moniliform swellings may, of course, modify nervous function, and to such changes may, perhaps, be attributed those losses of memory, slight manias, and melancholias that are now and then reported to follow prolonged anæsthesia in the human subject.

The Effect of Carbonic Acid upon the Central Nervous System. From his experiments on frogs and rabbits, Hans Winterstein¹ comes to the following conclusions: 1. That carbonic acid is a poison to the central nervous system. 2. Its effect depends upon a paralysis or a decomposition of the living substance. 3. The intensity and rapidity of the paralysis depends in a high degree upon the partial pressure of the carbonic acid, and seems to be proportional to it to a certain degree. 4. The carbonic acid acts excitingly upon the peripheral nerve organs. 5. The excitement preceding the paralysis or combining itself with it is purely of reflex origin.

The Physiological Effects of Extracts of Nervous Tissues. After confirming the findings of previous investigators, that the injection of extracts of nervous tissue produced a temporary lowering of blood-pressure, Halliburton² argues that this fall is due to choline. The experiments were made on cats with all kinds of nervous tissue, brain,

¹ Archiv f. Physiologie, 1900, Supplement Band, S. 177, .

² Journal of Physiology, vol. xxvi. p. 229.

spinal cord, sympathetic system, and general nerves. Cleghorn¹ found the same fall of pressure, but denied that it was due to choline. In fact, he removed the choline by precipitation with platinum chloride, and found the fall of pressure even after the administration of atropine. Halliburton repeated these experiments, and found the same result, but attributed it to a remnant of choline in the solution or to the depressing effect of platinum chloride itself. Halliburton does not claim that choline is the only substance of physiological importance in the extracts obtained, but he does claim that it is the only substance which can readily be identified there by which these results could be produced.

¹ American Journal of Physiology, vol. iv. p. 471.

HYGIENE.

By HENRY B. BAKER, M.D.

DURING the past year the most notable occurrences bearing upon the lessening of disease have been two: (1) The announcement at the London Congress relative to tuberculosis by so eminent a man as Dr. Koch of his belief that bovine tuberculosis is not dangerous to man, and (2) the working out in Cuba by Drs. Reed, Carroll, and Agramonte of the evidence that yellow fever is spread by a species of mosquito—*Culex fasciatus*, Fabr., *Stegomyia fasciatus*, Theobald.

The results of Dr. Koch's action are not yet very largely available, especially on his side of the question, and it may be several years before they become complete. The importance of the action rests in the very powerful stimulus which it has given and will continue to give to investigations having for their object the decision of the very important question raised by him.

BOVINE AND HUMAN TUBERCULOSIS.

The medical journals still teem with discussions and accounts of experiments made and to be made to determine whether or not bovine tuberculosis is dangerously communicable to man. But thus far an essential point appears to have been overlooked; thus mention is made¹ of experiments by Dr. Rokitsansky in a hospital of which Professor P. Baumgarten, of Tübingen, was pathologist, in which large quantities of bovine tubercle bacilli were injected under the skin of some half-dozen patients suffering from generalized malignant disease, with absolutely negative results. But it should be remembered that tuberculosis is not usually contracted in that manner, and that even after a large number of inoculation and injection experiments shall have been made, with both bovine and human tubercle bacilli, there must still remain the question whether or not the results would have been negative if the bacilli had been taken into the body in the way in which they are usually taken in when tubercular disease is contracted, namely, either

¹ Berliner klin. Wochenschrift for September 2, 1901; British Medical Journal, September 7, 1901.

by ingestion, or by inhalation, at such time of the year as the body is in the condition favoring the contraction of the disease, which in Michigan, and therefore presumably true in the Northern United States, is now conclusively proved by statistics to be in the spring of the year.

As long ago as 1894, G. Sims Woodhead said: "We must, therefore, agree with Koch and others that there are many cases in which although tuberculous virus is introduced into the tissues, especially near a cutaneous surface, it does not—for some as yet unexplained reason—multiply and set up a true infective and invading process. At the same time, it cannot be too strongly insisted that under certain conditions inoculation in the skin and subcutaneous tissue may be followed by a spreading, and even generalized infection."¹

So far as relates to experiments on the lower animals, tubercular bacilli from bovine animals seem to be more virulent than those from human sources. But results of inoculation experiments in animals or in man cannot be accepted as of any great value as evidence of the fate of bovine tubercle bacilli in the human body when ingested or when inhaled under conditions favoring their lodgement and propagation.

As indicated by Dr. Koch, the question, Is bovine tuberculosis dangerously communicable to man? cannot well be answered by direct experiment; therefore, it should be attacked by indirect methods; and Dr. Koch himself has made a start at such indirect investigation, but admits that the question cannot be decided to-day or to-morrow; yet, from superficial examination, he assumes that the extent to which bovine tuberculosis is conveyed to man is not great. Other men eminent in scientific pursuits have concluded that the extent of its conveyance to man is great; in fact, the medical and sanitary profession as a rule, with some notable exceptions, have assumed, on such evidence as came to the great mass of the profession, that bovine tuberculosis is a prominent source of human tuberculosis.

The fact that this question cannot be decided by experimental methods makes it a very proper question to be dealt with by the statisticians; and before the ultimate conclusion is reached, many statisticians, dealing with different classes of statistics, should be heard from. As one contribution to this study, it may be mentioned that in Michigan the statistics of deaths collected by the State Department show that the proportion of all decedents from so-called "consumption" is five times as great in the first five-year period of age as during the next five-year period. Inasmuch as children aged under five years are usually fed largely on milk, uncooked, to a very much greater extent than are children during the ages from five to ten years, and inasmuch as cow's

¹ *Lancet*, London, October 27, 1894, p. 957.

milk is known to contain, not very infrequently, the bacillus tuberculosis, while it is believed that in the milk of nursing women the bacillus tuberculosis is not often present, and inasmuch as the milk of tuberculous cows is well known to veterinarians to be a common cause of death of calves, it seems reasonable to believe that the extraordinary mortality of human infants from "consumption" may be, in part, due to the ingestion of milk of tuberculous cows.

And this belief is not destroyed by the assumption that because the death of the children was attributed to "consumption," and the tubercular disease was probably largely in the lungs, therefore, the bacilli must have entered the body by way of the air-passages, and not with the food. It is quite possible that the glands in the intestinal region may not permanently stop all the tubercle bacilli which enter by that route, and that the chyle emptied by way of the thoracic duct into the left subclavian vein may contain such bacilli, in which event they will tend to lodge in the first capillary system reached, namely, the lungs, and in that part of the lungs where the circulation is most sluggish, as, for instance, in the apices, just where inhaled bacilli would have little chance of reaching, and just where the first lodgement is commonly found in consumption of the lungs.

The foregoing facts and considerations make the fact that, according to the reports of the decedents from consumption in Michigan, five times as large a proportion are aged under five years as are aged from five to ten years, an interesting one in connection with the study of the relation of the milk of tuberculous cows to the causation of human tuberculosis.

But in order to negative the assumption by Dr. Koch that in predominant tuberculosis of the lungs the infection must have entered by the air-passages, it is not necessary to assume this somewhat direct channel of infection by way of the thoracic duct exclusively, because Dr. G. Sims Woodhead has actually traced the course of the invasion in numerous instances to have been by a much more indirect route than by the thoracic duct. He says: "I have seen in case after case in children, and in animals fed on tuberculous material, the lungs markedly affected, but in a large proportion of these cases it has been possible to trace the course of invasion back, from a caseous or old calcareous mesenteric gland, through the chain of retroperitoneal glands, up through the diaphragm to the posterior mediastinal and bronchial glands, and so on to the lung. I have not seen this in a few cases only, but in dozens of children, in a few adults, and in many animals."¹

It has been pointed out, also, that in order that the disease should be mainly in the lungs, it is not at all essential that the infection shall

¹ Lancet, London, 1894, vol. ii. p. 960.

enter as dust, because if in the food, and especially if in milk, it may lodge on the tonsils, and from there pass on by way of the lymphatics. Dr. G. Sims Woodhead has said: "In many of these cases the process can be traced from the glands in the tonsil down into the neck, and so on to the thorax, by the mediastinal and post-sternal glands, and by the intercostal lymphatics and glands; and it is interesting in such cases to note how the lungs may be perfectly healthy, until the glands at their root or in the pleura have become distinctly affected."¹ Many physicians have seen children with suppurating glands of the neck, formerly called "scrofulous" sores, and in many instances such children have grown to maturity without other evidence of tubercular disease, in which cases the bacilli must have been stopped in their course by the lymphatic glands in the neck. Tubercular nodules in the tonsils are not uncommon, and frequently are not followed by evidence of tuberculosis in other parts of the body. But when not stopped by the tonsils nor by the glands of the neck the course of the infection has been traced by way of the mediastinal and post-sternal glands and the intercostal lymphatics and glands to the pleura, root of lung, and finally to the lungs.

In the experiment mentioned at the London Congress on tuberculosis by Dr. Koch, in which human tubercular sputum was fed to pigs, he found, post-mortem, "here and there little nodules in the lymphatic glands of the neck, and in one case a few gray nodules in the lungs," not in the intestine or intestinal glands, as his hypothesis demanded.

It is not probable that hogs are usually infected with tuberculosis by means of infectious dust; in most instances the infection must enter with the food; and yet tubercular disease of hogs, affecting the glands of the neck and the lungs, is not uncommon. Dr. G. Sims Woodhead has stated: "But the pig, in which the glands of the neck and the spleen are specially affected."² Dr. Koch's experiment included only six pigs, and with the comparatively non-virulent bacilli of human tuberculosis; yet, taken with other evidence, it seems probable that his results typify the usual course taken by the bacillus tuberculosis when ingested by hogs; and, if so, that knowledge would tend to reinforce the evidence already collected relative to children. Further experiments along this line are quite possible, and should be made at once, because the modes and channels by which the bacillus tuberculosis usually enters and gains a lodgement in the body are very important facts to be definitely ascertained.

But so far as pigs are concerned, the subject has been quite thoroughly investigated. Several years ago Dr. G. Sims Woodhead wrote: "It is

¹ *Lancet*, London, 1894, vol. ii. p. 958.

² *Ibid.*, p. 959.

found when pigs are fed on tuberculous material held in solution, especially if the solution contains fatty or viscid material, that in a very large proportion of cases these animals become affected with tuberculosis of the glands associated with the tonsils. It has long been a well-known fact among veterinary surgeons that swellings at the angle of the jaw, often leading to abscess, were not uncommon in the pig; but it is only comparatively recently, especially in this country, that the tuberculous nature of this abscess and the relation of these swollen glands to a tuberculous process have been fully recognized. Abroad, in France, Denmark, Germany, and Holland, this is now so far accepted that every animal inspected is examined for enlarged glands or for any indication of a tuberculous lesion in the region of the tonsil, and especially near the cervical vertebræ, where the glands around the pharynx come in contact with the bony structures. As a result of such examination it has been found that tuberculosis in pigs is a much commoner disease than was at one time imagined."¹

At the autumn, 1901, meeting of the American Public Health Association, its Committee on Animal Diseases and Animal Food made a report in which the chairman, Dr. Salmon, of Washington, D. C., Chief of the Bureau of Animal Industry, U. S. Department of Agriculture, gave systematic attention to the recent doctrine of Dr. Koch relative to bovine tuberculosis. "In order to make clear what is already known preparatory to taking steps to definitely settle contested questions by experimentation," Dr. Salmon classified some of the evidence now on record and available under four heads: 1. Accidental inoculations with bovine bacilli. 2. Clinical evidence of individuals infected with milk. 3. Statistics of intestinal tuberculosis. 4. Results of post-mortem examinations. Under each of these heads he gave numerous facts, all tending to prove that bovine tuberculosis is dangerously communicable to man.

HOW YELLOW FEVER IS SPREAD.

One of the most important contributions to sanitary science in recent times has been the demonstration of the propagation of yellow fever by means of the blood of a patient, and particularly by a species of mosquito—*Culex fasciatus*, or, as recently named by Theobald, the English entomologist, *Stegomyia fasciatus*. "Unlike *Culex pungens*, this mosquito bites by day as well as during the night-time. Judging from my own experience, I should say that its favorite hours for feeding are from 4 P.M. to 10 P.M."²

¹ Lancet, London, 1894, vol. ii. p. 958.

² Walter Reed, M.D., Surgeon U. S. Army, Address, Medical and Chirurgical Faculty, Maryland, April, 1901; Medical Record, New York, August 10, 1901.

Dr. Reed and his associates,¹ in November, 1900,² "Proposed to attempt the infection of non-immune individuals in three ways, viz.: first, by the bites of mosquitoes that had previously bitten cases of yellow fever; second, by the injection of blood taken during the early stages from the general circulation of those suffering with the disease; and, third, by exposure to the most intimate contact with fomites."³

A very thorough trial of the last-mentioned way proved that it did not occur.

The attempts in both of the other ways were successful, four out of five persons contracting yellow fever by the subcutaneous injection of blood taken from the general circulation of a patient on the first and second days of the disease, and ten out of thirteen persons contracting yellow fever by the bites of mosquitoes infected by having bitten persons in the early stages of yellow fever. "Of the three negative cases, it will be observed that one (Case VI.) who had reacted negatively to the subcutaneous injection of 1.5 c.c. of blood on December 26, 1900, also reacted negatively to the bites of mosquitoes on January 8, 1901, and this, notwithstanding the fact that he was bitten by the very same insects which nine days before had infected Case VII. We have good grounds for this opinion, therefore, that this Spaniard may be looked upon as one who possessed a natural immunity to yellow fever, especially as he was the only one of five persons who did not develop the disease after receiving an injection of blood taken from the general circulation, and was also the only one of five non-immunes who did not contract yellow fever when bitten by insects which already had been proven capable of conveying the disease to other individuals."⁴

Dr. Reed and his associates found evidence that after a mosquito has bitten a patient sick with yellow fever a period of "about twelve days" elapses before that mosquito is capable of conveying the disease, by its bites, to a susceptible person; and Dr. Reed asks attention to the fact that in carefully observed and recorded outbreaks of yellow fever in the past in small settlements where the facts can be most accurately learned, "the interval between the infecting and secondary cases of yellow fever" has been such as to accord with this fact. Thus, the observations of Dr. Carter, of the United States Marine Hospital Service,

¹ James Carroll, M.D., and Aristides Agramonte, M.D., Acting Assistant Surgeons, U. S. Army.

² At Camp Lazear, near the town of Quemados, Cuba, the camp being named for a fellow investigator, the late Dr. Jesse W. Lazear, Acting Assistant Surgeon, U. S. A., who died of yellow fever while courageously investigating the cause of this disease.

³ Walter Reed, M.D., Surgeon U. S. Army, Address, Medical and Chirurgical Faculty, Maryland, April, 1901; Medical Record, New York, August 10, 1901.

⁴ Dr. Reed's Address at Baltimore, April, 1901; Medical Record, New York, August 10, 1901.

at Orwood and Taylor, Miss., in 1898, showed that "if we take all the secondary cases that occurred in those sixteen houses, we find that of a total of seventy-one cases only one developed the disease after so short an interval as eleven days and fifteen hours; in other words, seventy, or 98.5 per cent., of the secondary cases occurred after an interval of thirteen days."¹

However, Dr. Reed admits that "in our first successful experimental case, where the disease was produced by the bite of the mosquito on the twelfth day after the insect's contamination, we could not say, of course, that this particular mosquito would not have conveyed the infection had it been allowed to bite on the eleventh or tenth day after contamination."

This point is a very important one in the practical work for the restriction of yellow fever; because, if in each outbreak there are twelve days, or even ten days, after the initial case, within which time infected mosquitoes may be destroyed by disinfection of infected premises, and the patient protected from further bites and consequent liability to spread the disease, it is exceedingly important that this fact be known; it is just such knowledge which will enable the practical sanitary official to restrict the outbreak to the initial case.

In fact, it is the belief of Dr. Gorgas, of the United States Army, the present efficient head of the Sanitary Service in Havana, that to action upon this knowledge is due the fact that yellow fever has been practically restricted in Havana during the past few months.

Another practical question which seems to have been settled by the experiments made by Dr. Reed and his associates is the period of incubation of yellow fever. The average period of incubation of the sixteen cases of experimental yellow fever was eighty-seven and one-quarter hours, or three days fifteen and one-quarter hours. "If we separate the twelve mosquito infections from the four cases produced by the injection of blood we have for the former a period of incubation of ninety-four hours, or three days and twenty-two hours, and for the latter an incubative stage of sixty-seven and a half hours, or two days nineteen and a half hours. The average period of incubation, therefore, in the cases brought about by subcutaneous injection of blood was shorter by twenty-six and a half hours than those occasioned by the mosquito's bite. By the former method this stage varied from forty-three hours to ninety-four hours, while in the mosquito infections the shortest incubative period was seventy and the longest one hundred and forty-six hours. If we accept those cases produced by the mosquito's

¹ Dr. Reed's Address at Baltimore, April, 1901; Medical Record, New York, August 10, 1901.

bite as the usual method of propagation of this disease, it will be observed that of the twelve cases one occurred on the third day, nine on the fourth day, one on the sixth day, and one at the beginning of the seventh day after incubation.

"While our results, therefore, confirm the statement of later writers that the period of incubation of yellow fever does not usually exceed four or five days, they also seem to indicate very plainly that this stage may be prolonged more frequently, perhaps, than had been supposed.

"In 16.6 per cent. of our cases the period of incubation exceeded the usual quarantine period of five days. If we add Carter's cases to those observed by us we find that of twenty-four cases the period of incubation exceeded five days in three, or 12.5 per cent. We will not further dwell on this subject than to remark that Cases II. and IV. of Table I. could have passed quarantine on the morning of the sixth day after inoculation, with a clinical thermometer under the tongue, without exciting any suspicion by reason of the presence of fever."¹

From the experiments relating to the period of incubation of yellow fever in man (one and two-thirds to six and one-twelfth days), and the period elapsing after the infection of the mosquito before it is capable of inoculating the disease in man (ten to twelve days), taken in connection with the observations by Dr. Carter in Mississippi in 1898, that out of seventy-one secondary cases, one occurred on the thirteenth and one on the twelfth day, an inference may be drawn that in the practical work for the restriction of yellow fever what is to be done must be done as soon as possible after the discovery of a case, and certainly within ten days from the occurrence of the first case.

Drs. Reed, Carroll, and Agramonte give as one of their eleven conclusions: "The spread of yellow fever can be most effectually controlled by measures directed to the destruction of mosquitoes and the protection of the sick against the bites of these insects."²

THE BEARING OF KNOWLEDGE OF THE SPECIFIC CAUSE OF A DISEASE.

One of the main purposes of gaining, and perhaps the greatest usefulness of, accurate knowledge of the nature of the specific cause of a disease is to enable us to have clear ideas of the modes by which the disease is spread and how it may most effectively be restricted or prevented. If, as is true of smallpox, we already have clear and complete

¹ Transactions of the Association of American Physicians, 1901, vol. xvi.

² Etiology of Yellow Fever, an Additional Note, Pan-American Medical Congress, Havana, February, 1901; Journal of the American Medical Association, February 16, 1901.

knowledge of how the disease is spread and how it may be restricted or prevented, then knowledge of the cultural peculiarities of the specific cause in artificial media is of little prospective value compared with such knowledge relative to a disease like consumption at the time its specific cause was discovered by Dr. Koch, or like yellow fever a year or more ago, when effective work for the prevention of the disease could not be undertaken for lack of knowledge of its modes of spreading, knowledge which is now public property, that relative to consumption having come largely through the discovery of the specific cause, while that relative to yellow fever has come through investigations directly relating to its modes of spreading.

Without doubt the establishing on a sound scientific foundation of the nature of the specific cause of yellow fever may yet be expected to be of value to humanity ; as much may be expected from the establishing of the nature of the specific cause of smallpox ; yet the main purpose for which that knowledge has heretofore been wanted relative to yellow fever has, apparently, been accomplished through the investigations made by Drs. Reed, Carroll, and Agramonte.

THE RESTRICTION AND PREVENTION OF INTERMITTENT FEVER.

Progress has been made in perfecting and systematizing efforts for the restriction of the spread of intermittent fever by the destruction of the larvæ and of the breeding-places of mosquitoes by wire-netting screens on windows and doors, and by the use of quinine.

In this country very thorough work has been done by Dr. Doty, Health Officer of the Port of New York, who selected a district on Staten Island where a house-to-house inspection of about a hundred small wooden houses showed that at least 30 per cent. of the inhabitants were suffering from the acute or chronic form of malarial fever, and where within an area of a square mile were twenty-five stagnant pools varying from five feet in diameter to an acre or more in area. *Anopheles* mosquitoes, of the malarial variety, were proved to be present, and bacteriological examination of the blood of a patient showed the presence of the malarial parasite. Many tests were made to ascertain the effectiveness of various substances for the destruction of the mosquito larvæ. Dr. Doty claims "that petroleum oil will surely and promptly destroy mosquito larvæ, and, so far as careful experiments indicate, it is the only agent which can be depended upon for this purpose." "Municipal sanitary codes should include strict regulations not only against the existence of stagnant pools, but of all forms of breeding-places, and

should empower sanitary officers to employ such means as are necessary to protect the public against these insects, and, when required, the application of oil should be made under their direction. In order to make this work uniform and effective, the co-operation of the State and Federal authorities is absolutely necessary, and such action would be followed by the most gratifying results."¹

In other countries efficient work has been done, fostered by associations, philanthropic individuals, and, in a few instances, by governments. The Italian Society for the Study of Malaria has vigorously investigated in seventeen provinces where malarial disease was epidemic, and several foreign governments have sent delegates there to study the subject.

Major Ross has lately returned to England from Africa, where he has been on his fifth expedition, sent out by the Liverpool School of Tropical Medicine. He had accepted a large sum of money, contributed by philanthropic persons, to pay for practical work in Sierra Leone, and the work has been commenced with every prospect of success. "He had witnessed the rapid and successful filling up of marshes by sand from the lagoons, and the rational utilization of gaol prisoners for this useful work. He had inspected numerous houses rendered mosquito-proof by fine wire-netting, which, while it did not exclude the breeze, as he expected it would, did exclude insects."² "The Governor supplied men and the necessary implements, charts, etc. One gang was employed in destroying mosquito larvæ in houses and surrounding areas. These laborers in thirty-four days cleared 2473 houses and removed 358 cartloads of broken bottles, tins, and other débris in which the *culex* mosquito breeds. Another body of men have been engaged in draining the breeding-pools of the *anopheles* mosquito and in destroying their larvæ by means of oil. As to the result of these efforts, Major Ross said it was too early yet to speak emphatically, but the number of mosquitoes in the centre of the town had certainly been largely reduced. There were hardly any to be found in Dr. Logan Taylor's house, where formerly they used to swarm. The same state of affairs prevailed at Government House, where Major Ross was living with the Governor. Dr. McKendrick, of the Indian Medical Service, who had been deputed to watch over the operations of the expedition on behalf of the Government of India, was not bitten once during a whole month. In former days he would certainly have been bitten at least five or six times a day. Major Ross said he had no doubt that the expeditions would be successful, and that they would be continued as long as necessary."³

¹ Boston Medical and Surgical Journal.

² British Medical Journal, September 7, 1901, p. 644.

³ Ibid.

A NEW VIEW OF THE NATURE OF TYPHOID FEVER, AND THE INTERNAL USE OF A NEW GERMICIDE.

At the autumn, 1901, meeting of the American Public Health Association, Dr. Eugene Wasdin, of the United States Marine Hospital Service, read a paper setting forth the view that instead of entering the body by way of the intestines, as has been the view of physicians and sanitarians in recent years, typhoid fever is generally spread through the air, and enters the body by way of the lungs.

It will be remembered that for many years—in fact, until his death—Pettenkofer strongly advocated this view.

Dr. Wasdin says : “ It is no more primarily a disease of the intestine than smallpox is a disease primarily of the skin. The clinical symptoms most constant in the disease, and which point to colonization of the bacillus of Eberth, are not those of the intestine, but are found in the lungs. The symptoms of lung invasion are early, those of the intestine are later. In natural infections with this bacillus it must be primarily located at some point of colonization (incubation), and it is from this point that the organism enters the circulation, this invasion depending upon the development of its potential of septicity. This septic stage in typhoid arises *before* the end of the first week of illness, while the germ is scarcely ever found in the intestinal contents until after this time, when it may also be found in the urine. Toxic vasomotor paresis is the early symptom in the disease, accompanied by hemorrhages into the hollow organs, such as the stomach, intestine, bladder, uterus ; and attention is directed to the coincidence in time of these probable hemorrhages and the presence of the bacillus in the stools. The presence of the bacillus in the blood does not seem of extreme importance ; the primary colony endangers the patient. Terminal infection of the lungs is rare ; such terminal infection is found in the serous or lining membranes, or in the bones. The infection in typhoid fever is, then, in the majority of cases, *not* by the way of the alimentary canal, and therefore personal and municipal hygiene should demand a careful consideration of the convection of the organism by the air, its entrance into the respiratory tract, and resulting infection. The treatment of typhoid fever should no longer be limited, as at present, to the elimination of the germ products, but should include active attack upon the germ in its primary colony as well as in the secondary intestinal colony ; and, since death from typhoid fever, except in the *rare siderante cases*, is almost always due to intestinal or lung fatalities, the control of these will reduce the mortality and at the same time the duration of the disease.”

For the "active attack upon the germ in its primary colony," Dr. Wasdin has used, in a considerable number of cases, and he thinks with success, the new organic disinfectant, "benzozone," invented by Professor F. G. Novy, of the University of Michigan. This organic peroxide is a powerful germicide, apparently innocuous to man and other animals. But the details have not yet been published by Dr. Novy.

THE RESTRICTION OF DISEASE BY LICENSED EMBALMERS.

During the year just passed noteworthy progress has been made in a movement of considerable prospective importance to the public health throughout the United States, namely, the bringing under the exclusive supervision of expert embalmers and disinfectors the preparation of all corpses dead of dangerous communicable diseases to be transported by railroad. Several States have been added to the number in which this is now provided for. Michigan is one of the latest. Although the movement had its first impulse in that State many years ago, it is only since the taking effect of a law passed at the last session of the State Legislature that the system has there been inaugurated. Hereafter, in that State as heretofore in several other States, by a rule of the General Baggage Agents' Association, no corpse of a person dead of a dangerous communicable disease will be accepted for transportation unless certified by the local health officer to have been disinfected and prepared for transportation by an embalmer licensed for such purpose after an examination in anatomy, disinfection, and embalming, by the State Board of Health.

Wonderful progress has been made by funeral directors and embalmers in recent years ; but the passage of such a State law, at their instance, providing that all who are to prepare infected bodies for transportation shall submit to examination by a State Board of Health, in anatomy, disinfection, and embalming, the carrying out of the entire plan being at the expense of the embalmers themselves, is a movement for the public welfare which is unique and worthy of strong commendation.

The far-reaching consequences of such action can hardly be appreciated from a plain statement of the facts, without mention of some of the attendant circumstances ; for instance, in Michigan, recently, the State Association of Funeral Directors maintained for several days expert teaching in a school of instruction for embalmers, at the close of which school about four hundred of the embalmers took the examination before the State Board of Health. That results in about four hundred men scattered throughout the State who from that time on are trained in the methods for the restriction of dangerous communi-

cable diseases. And those four hundred men are of those who are to have to do with corpses of persons dead of those diseases. Similar work has been done in other States.

Thus, knowledge relative to modes of spreading of diseases, disinfection, and other restrictive measures, which until recently has been in the possession of physicians only, is, through this new movement, coming to control the daily work of hundreds of men in each State in which this movement is in progress ; because the same men who are licensed to prepare corpses for transportation are also those who are to do most of the preparing of corpses for burial without transportation.

Again, these same men are the same as have to do with the very beginnings of mortality statistics, because such statistics must start with the burial permit.

MORTALITY STATISTICS.

Beginning with the year 1901 a large number of States and cities have joined in the adoption of a uniform and thoroughly comparable classification of causes of death, namely, the Bertillon system as revised by an International Commission of Revision at the Congress of Hygiene and Demography at Paris, 1900. This system is now predominant in Europe and North and South America, and will afford great advantages to sanitarians in enabling them to make precise comparisons of mortality and morbidity statistics in different countries. A translation of the revised classification was published by the Surgeon-General of the United States Marine Hospital Service at Washington early in the year.

The preliminary results of the mortality statistics of the United States Census of 1900, recently published, show a gratifying diminution of the death-rate in the registration area of the United States compared with ten years ago. Unfortunately, this area does not cover the entire country, and the data derived from a single year's observation may be more or less exceptional. It is desirable that the census authorities co-operate with State and municipal sanitary and registration offices throughout the country in order to secure an extension of the area of satisfactory registration of deaths in the United States, and the adoption of fairly uniform and comparable methods for this purpose ; also, that the mortality statistics of this country shall be under expert supervision in some office in Washington which shall be permanent and not periodical once in ten years, as the census has been.

What may prove to be an important start in this direction is the work of the United States Department of Labor, under a paragraph in an act of Congress which became a law July 1, 1898, but which is now just beginning to exhibit useful results. The paragraph is as fol-

lows: "The Commissioner of Labor is authorized to compile and publish annually, as a part of the *Bulletin of the Department of Labor*, an abstract of the main features of the official statistics of the cities of the United States having over 30,000 population." The report just issued (dated September, 1901) includes four tables relative to deaths: Deaths by causes, percentage of deaths from each specified cause, death-rate per 1000 population by causes, death-rate per 1000 population.

Such statistics, however, should be compiled and published under the supervision of an expert in that class of vital statistics, and, together with editorial comments, should be printed in a separate volume.

Another effort by an official of the United States toward mortality statistics is that by the United States Marine Hospital Service. In a recent number of its *Public Health Reports*, published in accordance with an Act of Congress approved February 15, 1893, is a table of mortality statistics of 1190 cities and towns in the United States for the year ending December 31, 1900, compiled from answers received to a circular letter sent to cities and towns having a population of 1000 or more. Attention was called to the two columns showing the annual mortality-rate per 1000 of the population, one column being based on the estimated population, and the other upon the population according to the United States census of 1900. The population represented was, according to the census, 20,712,608, but it was estimated locally at over 770,000 more than was shown by the census.

This compilation is unsatisfactory, however, owing to the failure of the compiler to secure statistics from States and cities known to have accessible data. Thus, for Michigan, no deaths are given for Detroit, Grand Rapids, or other important cities, although a full statement of mortality might have been given for every city and county of the entire State.

Whatever department of the United States Government finally succeeds in establishing useful mortality statistics of this country, in order to make them most useful it must co-operate freely not only with the officials in charge of the mortality statistics of cities and towns, but also with those in charge of such statistics in the several States.

THE BACTERIAL TREATMENT OF SEWAGE.

During the past year one important modification has been made in this country, as noted further on. Aside from that, not much advance has been apparent in this comparatively recent method of purifying sewage; yet an important conclusion has been reached by one promi-

nent American sanitary engineer,¹ who, for a few years, has been experimenting in this work, namely, that much remains to be learned as to the nature and means for overcoming local conditions, which he has found to greatly modify the results of this method of attempting the purification of sewage by the action of the anaërobic bacteria in air-tight "septic tanks," and then by the action of the bacteria in "contact beds" of coke.

Extensive experiments at London, England, under the direction of Professor Frank Clowes, chemist of the London County Council, proved that the bacteria were reduced by 27.7 per cent., the spores by 38 per cent., and the liquefying bacilli by 11.3 per cent.; yet "that by treatment in contact beds there is no reduction in the number of certain pathogenic bacteria contained in the sewage, such as *bacillus coli communis*, and the spores of *bacillus enteritidis sporogenes*."² The most important bacterium pathogenic to man—*Eberth bacillus*—might then be expected to pass through this process undestroyed.

Yet it is too early to conclude that the "septic tank" system of sewage treatment, or some modification of that system, is not to become capable of yielding valuable results, even in the way of lessening the spread of the pathogenic bacteria. The system is still in its infancy.

The advantages of bacterial over chemical treatment of sewage have been summarized by Professor Clowes as follows:

"1. It requires no chemicals.

"2. It produces no offensive sludge, but only a deposit of sand or vegetable tissue which is free from odor.

"3. It removes the whole of the suspended matter, instead of only about 80 per cent. thereof.

"4. It effects the removal of 51.3 per cent. of the dissolved oxidizable and putrescible matter, as compared with the removal of 17 per cent. only, effected by the present chemical treatment.

"5. Further, the resultant liquid is entirely free from objectionable smell, and does not become foul when it is kept; it further maintains the life of fish."³

Very recently this subject has been forwarded in an important manner by supplementing the septic tank and contact beds by intermittent downward filtration through specially constructed sand filters. The effluent, as it enters the river, is clear and bright and without a suspicion of sewage in its appearance.⁴ The bacteriological results have not yet been published; but previous experiments at Lawrence, Massachusetts, lead to the belief that this method should yield good results.

¹ Alvord, of Chicago.

² D. H. Bergey, M.D., *University Medical Magazine*, Philadelphia, December, 1900.

³ *Ibid.* ⁴ "The Municipality," *Madison, Wis.*, October, 1901, pp. 126-129.

This plant, "which, in its method of operation, is the first of its kind in this country,"¹ is at Wauwatosa, a residence suburb of Milwaukee, Wisconsin, and a city of about three thousand inhabitants. The cost of the plant was a little over ten thousand dollars.

The engineers, Alvord and Shields, the well-known sanitary engineers of Chicago, have been retained, in an advisory capacity, until May 1, 1902; therefore, the details of the working of the plant are likely to be observed and reported upon later.

Because of the thousands of places where the sewage pollution of streams should be prevented, it is to be hoped that this system may soon be proved to be so far perfected as to be practicable for adoption.

¹ "The Municipality," Madison, Wis., October, 1901, pp. 126-129.

PRACTICAL THERAPEUTIC REFERENDUM.

BY E. Q. THORNTON, M.D.

Acetopyrine is a white, crystalline powder, sparingly soluble in cold water, but soluble in warm water and readily soluble in alcohol. It is a synthetic product made by combining antipyrine with aspirin. Its dose is from 5 to 30 grains (0.30 to 2 grammes). It should not be prescribed in combination with alkalies nor substances incompatible with antipyrine.

Josef Winterberg and R. Braun¹ employed acetopyrine in the treatment of rheumatism, and believed it to be superior to sodium salicylate or other salicylic-acid derivatives.

It is preferably prescribed in the form of powder, capsules, or cachets.

R.—Acetopyrini 3j. gm. 4.00
Pone in capsulas No. xii.
Sig.—One to two capsules three times a day.

Ammonium Persulphate. The studies of Drs. Mazyck P. Ravenel and S. H. Gilliland² with ammonium persulphate, which until in recent years has been too high in price to make it available as a practical disinfectant, show that it possesses decided bactericidal properties and is a valuable deodorizer. By using solutions of various strength they were able to kill the micro-organisms of typhoid fever and ordinary pus microbes in from fifteen to twenty minutes to one to two hours.

Anthrax spores were killed by 5 per cent. solution in thirteen hours. In many cases they found it to be superior to carbolic acid as a germicide. The color in ribbons of delicate shades are not affected by immersing them for two hours in 10 per cent. solution of the salt.

Antiplague Vaccine and Curative Seræ. Haffkine prophylactic plague vaccine continues to be employed with increasing confidence as a protective against infection by bubonic plague wherever the disease has appeared. It confers immunity for a short period only, and, therefore, during the continuance of an epidemic frequent vaccinations at intervals of from fifteen to twenty days are required. The usual quantities considered necessary at each injection are, for males twenty-five years or over, 5 c.c. (m.lxxv); for twenty years or over, 4 c.c.

¹ Wiener klin. Wochenschrift, September 27, 1900.

² University Medical Magazine, February, 1901.

(m_{lx}); for fifteen years or over, 3 c.c. (m_{xliv}); for ten years or over, 2 c.c. (m_{xxx}); for five years or over, 1 c.c. (m_{xv}). Females require one-fifth less than males of the same age. As the prophylactic is liable to rapidly deteriorate soon after the bottle containing it is opened, it is considered unsafe for use if it has been exposed for over two hours. The curative seræ of Yersin-Roux and of Lustig have been employed with apparently good results in many cases of bubonic plague, but the mortality-rate still ranges very high.

Antipneumococcic Serum. This substance consists of the blood-serum obtained from animals previously immunized by injecting first dead and then living cultures of pneumococci. The fluid is probably neither antibactericidal nor antitoxic, and is without power to influence the exudate in the lung. It is said to be anti-infectious and its possible power for good to depend upon the property of lessening the extension of the infection and preventing sepsis. Laboratory experiments show that when an animal is injected with a living culture of pneumococci it dies from sepsis; but if the antipneumococcic serum is mixed with a living culture of pneumococci and injected, sepsis does not follow, and the animal's life is preserved. In fact, it has been shown that the serum will preserve animals from many times the ordinary fatal dose of a virulent culture of pneumococci. Although these experiments would indicate that the serum is of great value in the treatment of acute croupous pneumonia, clinical applications have failed to show that it is of any decided utility.

G. E. Tyler¹ reports six cases of pneumonia (with one death) in which the serum was employed in conjunction with ice-packs to the chest, strychnine, alcohol, and digitalis as needed, and oxygen inhalations in desperate cases. He also gives statistical reports of 121 cases treated by the serum, in which there were twenty deaths, a mortality of 14.18 per cent. In addition to the eighteen cases reported by J. C. Wilson,² in which there were four deaths, or 22 per cent., in collaboration with Page³ he makes another report of seventeen cases treated (in the German Hospital in Philadelphia) with the serum, conjoined with the usual methods, and in this last series six of the seventeen died, a mortality of 33.3 per cent. The serum, which was obtained fresh, was administered in doses of 20 c.c. every three or four hours; the total quantity given varied from 80 to 1000 c.c. They state that the effect on temperature and respiration was not marked, and that in a few instances drowsiness followed the injection, and that in two cases it was necessary to abandon the treatment on account of the pain and restlessness in-

¹ Journal of the American Medical Association, June 1, 1901.

² Ibid., September 8, 1900.

³ Therapeutic Monthly, July, 1901.

cident upon it. In concluding their paper they say that their observations (based upon thirty-six cases in their service in the German Hospital) have not encouraged them to continue the use of the serum in croupous pneumonia. Including their own cases, they have collected reports of thirty-five in which the serum was employed, where there were twenty-seven deaths, a mortality of 16.6 per cent. Dr. Newton Snively¹ reports six cases of pneumonia treated by the serum. There was one death, or a mortality of 16.70 per cent. He is favorably impressed with its use in these cases, and believes that "it lowers temperature, relieves pain, ameliorates symptoms, shortens the attack by hastening the crisis, brightens the patient, and starts him earlier and more surely on the road to recovery." He thinks that in private practice, where the cases are seen earlier and are usually well nourished and not overworked, the remedy will be found of the greatest value.

Antistreptococcic Serum. Antistreptococcic serum has now been employed five or six years in the treatment of septic infections. It is a fairly well-established fact that in cases of pure streptococcic infection it will clear these micro-organisms from the blood and combat the deleterious influence of their toxins. It is useless in the treatment of other infections, and, as the serum is not entirely harmless, it should not be employed unless there is evidence that the symptoms are induced by streptococci. We constantly see reports condemning its use where evidently no pains have been taken to determine whether the case was one of mixed infection, or if streptococci were present at all, and, of course, such reports are valueless.

A. J. Primrose² reports two cases of puerperal sepsis in which the serum was employed with successful results. He injected 10 c.c. doses of the serum at intervals of twelve hours. The fever rapidly abated, and convalescence was promptly established. E. E. Montgomery³ believes that many failures in the treatment of streptococcic infection by the serum should be attributed to the use of an old preparation. In cases of puerperal sepsis where the associated erysipelatous manifestations render it evident that the streptococcus is the micro-organism to be combated the serum has been exceedingly beneficial. The quantity to be employed and the frequency of its administration depend on the virulence of the attack. From 10 to 30 c.c. can be given twice daily, as the condition demands. Frank A. Higgins⁴ used the serum in five cases (two of which died) of severe puerperal sepsis, and was not impressed with its curative value. He does not think it a safe procedure to use

¹ Therapeutic Gazette, June 15, 1901.

² New York Medical Journal, May 25, 1901.

³ American Medicine, April 6, 1901.

⁴ Boston Medical and Surgical Journal, May 2, 1901.

more than 10 c.c. every twelve hours, and, if no improvement is shown from the injection of from 40 to 60 c.c. during two or, at the most, three days, it should be discontinued. In Ludwig Knapp's¹ experience the results obtained from the use of the serum in puerperal infection have been either doubtful or absolutely negative. He injects 10 c.c. at the first dose, and if the results are negative the dose is repeated after twelve hours, and a third one given twelve hours later, if necessary. W. W. Keen² employed the serum in a case of streptococcic infection following a resection of the chest wall for large sarcoma, and the results were satisfactory.

Apocodeine Hydrochlorate is a yellowish, amorphous powder, freely soluble in water and alcohol. It is made by heating a mixture of hydrochloric acid and codeine contained in hermetically sealed tubes, in a similar manner to which apomorphine is made from morphine. It has been employed hypodermically in doses of from $\frac{1}{10}$ to 1 grain (0.006 to 0.06 gramme) as an expectorant and also as a laxative. Raviart³ speaks favorably of its action when given hypodermically in doses of 4 centigrammes. In none of the thirty-five cases reported by him in which the drug was employed were there any untoward effects. He considers the drug distinctly laxative rather than purgative, and found it to possess sedative and hypnotic power and stimulating to the glandular system, and also promotes intestinal peristalsis. At the Congress of Alienists of Bordeaux, Toy spoke very favorably of this remedy for quieting maniacal patients and also in inducing sleep. Aside from these beneficial properties, it acted as a gentle laxative. In none of his cases did vomiting or any untoward effect manifest itself.

The formula suggested by Raviart is as follows :

R.—Apocodeinæ hydrochloratis	gr. vij.	gm. 0.05
Aquæ dest.	℥ xij.	gm. 50.00
Misce.	Sig.—Use eighty minims hypodermically at bedtime, or as required.	

Atropine. Though not borne out by previous experimental study or clinical observation, there appears to be a very general impression that atropine is a certain and powerful respiratory stimulant, and it is quite extensively and in many instances freely employed as a physiological antagonist to opium in cases of poisoning by this substance. In a recent carefully prepared, highly scientific, and eminently practical paper, Dr. Edward F. Reichert⁴ records the results of experiments made by himself and others to determine the physiological effects of atropine upon the respiration, circulation, and heat functions in normal and morphin-

¹ Prager med. Wochenschrift, May 9, 1901.

² Journal of the American Medical Association, June 1, 1901.

³ Echo de Méd. Lille, December 2, 1900.

⁴ Therapeutic Monthly, May, 1901.

ized animals, and also the action of atropine upon these functions in normal and morphinized man. In its effect upon respiration he does not consider atropine either a reliable, prompt, or powerful stimulant, but believes it to be very unreliable and of ordinary power, and a drug which acts less frequently (as a rule) as a respiratory stimulant than otherwise. He quotes Mitchell, Keen, and Morehouse,¹ who asserted that in many instances the respiratory rate fell or remained unaltered after administration of atropine, and Harley,² who stated that exhibition of medicinal doses had no effect whatever. The experimental work of Harley, Bezold and Bloebaum, Meriot, Orlowski, Wood and Cerna, and Reichert upon the effects of atropine on respiratory rate in normal animals, and of Huebach, Lenhartz, Orlowski, Unverricht, Bing, Volmer, Wood and Cerna, and Reichert upon the effects of atropine on respiratory rate and volume in morphinized animals, is reviewed and harmonized. Attention is directed to the exciting effect of atropine upon the respiratory centre and its powerfully depressing effect upon the pulmonic (motor) fibres of the vagi. As a result of his observations upon man and experiments upon the lower animals, Reichert is led to agree with Lenhartz and Unverricht and others, who believe that in cases of morphine poisoning atropine does not usually excite respiratory activity, but, as a rule, actually lessens it. In his experimental study upon normal dogs Reichert found the action of atropine upon the circulation was very complex and uncertain, and that, as a rule, the administration of small doses caused an increase of pulse-rate and arterial pressure, while large doses caused a decrease in both, but that it was impossible to predict after any given dose how the pulse-rate would be affected. There was no constant relation between pulse-rate and arterial pressure, the rate increasing in some cases while pressure fell, and *vice versa*.

In pointing out the uncertainty of the action of atropine on the circulation in man he cites the observations of Mitchell, Morehouse, and Keen, and of Putnam,³ who state that after medicinal doses they have seen the pulse-rate fall and remain below the normal for a number of hours. From studies upon morphinized dogs he draws the deduction that small doses of atropine were antagonistic to morphine in its circulatory effect during the first or second stage of opium poisoning, but that in the third stage small doses were useless and large doses distinctly harmful.

Upon normal dogs he found that there was rarely a rise in temperature unless the dose was so large as to cause marked tremors or other motor disturbances; while in the morphinized dogs it increased the

¹ American Journal of the Medical Sciences, 1865, vol. i. p. 67.

² Old Vegetable Neurotic, 1869, p. 241.

³ New York Medical Journal, 1873, vol. xviii. p. 249.

general depression of metabolism, but somewhat hindered the fall of temperature caused by overdoses of morphine. These experiments upon dogs, however, are at variance with what is commonly observed in man; for no reasonable doubt can exist as to the fairly constant action of atropine in raising the body temperature. In a most careful study and review of the physiological action of atropine, and after comparing its physiological action with that of morphine, he calls into question the value of atropine in cases of morphine poisoning, and asks if atropine is valuable, or is it dangerous in cases of morphine poisoning. He states that the belief that "morphine and atropine are to a wide extent antagonistic was founded upon most superficial knowledge of their physiological properties. That they are in certain important respects synergistic is beyond question. Both are narcotics; both behave like double poisons, one acting as a general excitant and the other as a general depressant. Both cause in man a primary stage of psychical excitation, a secondary stage of psychical and physical depression; both primarily excite and secondarily depress the respiratory centre, the heart, the cardio-inhibitory apparatus, and the vasomotor mechanism. Both primarily increase and secondarily decrease the arterial pressure, the pulse-rate, and probably the secretory activity in general; both markedly lessen general metabolic activity and lower body temperature when given in moderate to large doses; both are delirifacients, hypnotics, paralyzants, and convulsants; both cause severe motor depression, which is particularly marked in the hind legs; both depress the sensory and motor nerves; both, in small doses, lessen, and in toxic doses excite, peristalsis; both cause death almost invariably by paralysis of the respiratory centre." He believes that a non-lethal dose of morphine may be made lethal by a sublethal dose of atropine. In proof of this he administered subcutaneously, to three dogs, two-thirds of the mean minimum lethal dose of morphine; to three others, one-third the mean minimum dose of atropine; and to six other dogs the same quantities of both alkaloids. All of the morphinized dogs recovered; all of the atropinized dogs recovered; but all of the six dogs receiving both morphine and atropine died.

These experimental studies of Reichert upon animals are very impressive, but are not in themselves convincing as to the exact value of atropine in morphine poisoning in man. When viewed, however, in connection with the collective statistics of Lenhartz referring to 132 cases of opium poisoning, some of which were treated with atropine and others not, the death-rate being 38 per cent. in those receiving atropine, and only 15 per cent. without, we are strongly led to agree with him in the belief that more deaths from opium poisoning treated by atropine result from the so-called antidote than from the opium.

It is suggested that atropine has been proven of value beyond doubt when administered in small doses during the first or second stage of opium poisoning, but it is distinctly harmful if given in large doses during any stage of the poison, and dangerous in any dose if given after the second stage.

From the recent and rather voluminous literature we are led to assume that many German physicians are using atropine in large doses, with very satisfactory results, in the treatment of intestinal obstruction. No good results can be expected to follow its use when obstruction is due to a constricting band of adhesions; but the clinical reports of its being used successfully when obstruction resulted from hardened fecal masses, strangulated or incarcerated hernia, invagination, and spasmodic conditions resulting from painful affections are numerous. It should not be looked upon as a substitute for surgical procedures; but there are cases where operations are refused by the patient or his friends, others in which operations must be deferred for some hours, either on account of the critical condition of the patient or from various causes; and by the use of the remedy in such cases no harmful results could follow, while its administration, by relieving vomiting, quieting pain, and promoting peristalsis, may possibly change the whole aspect of the case. That atropine is a valuable remedy when combined with laxatives is a well-established fact. In small doses it has the tendency to produce relaxation in the muscular layers of the intestines, and in large doses paralyzes the inhibitory fibres of the splanchnic nerves of the gut, thereby increasing peristaltic movements. Its value in the treatment of constipation was recognized by Trousseau forty years ago, who spoke of the drug in constipation as "*efficacité mer veilleuse*." Dr. Batsch¹ is one of the most enthusiastic advocates of the administration of full doses of atropine in treating ileus, and reports three severe cases, all of which under ordinary circumstances would have come to surgical operation. By the use of atropine two of these cases were brought to favorable terminations without operations. The third case was finally operated on and relieved by freeing a knuckle of a gut from an adhesion formed by a constricting band; but it was thought that the atropine, which had been used prior to the operation, was of value in sustaining the strength of the patient before, during, and after the operation, and also led to a satisfactory movement of the bowels twenty-four hours later. His first case was that of a woman, aged sixty years, who, for eight days prior to the day on which he saw her, had been treated with the ordinary laxatives without avail, and for two days had been annoyed by fecal vomiting. Although

¹ *Münchener med. Wochenschrift*, July 3, 1900.

laparotomy was urged by his associates, he advised that the operation be deferred for at least twenty-four hours, and suggested that in the meantime the patient should be prepared for laparotomy, and 0.002 gramme ($\frac{1}{80}$ grain) of atropine should be administered hypodermically at once and repeated in twelve hours if the bowels had not been moved in that time. His advice was followed, and after the second dose of atropine the vomiting ceased, the patient slept during that night, and the following morning there was a large bowel movement, and the patient rapidly recovered without surgical interference. The second case was that of a man, aged thirty-five years, suffering from fecal vomiting. Laparotomy had been advised, but the operation was deferred until atropine had been tried; 0.005 gramme ($\frac{1}{20}$ gr.) of atropine was administered subcutaneously during the morning. The vomiting ceased, the abdomen became flaccid; but as there had been no movement of the bowels by the evening, another dose of 0.005 gramme ($\frac{1}{20}$ gr.) was administered. At four o'clock the following morning the patient had several large bowel movements. The third case was that of a woman, aged forty-five years, who suffered with severe abdominal pains and constipation. She was not relieved by the usual laxatives, and vomiting now became active; 0.005 gramme ($\frac{1}{20}$ gr.) of atropine was administered. Although improvement appeared by the following morning, the patient being somewhat relieved of pain, another dose of 0.005 gramme ($\frac{1}{20}$ gr.) was administered; and on the same afternoon, as no dangerous symptoms were present and the patient felt better, another dose of 0.005 gramme ($\frac{1}{20}$ gr.) was given. The woman rested fairly well that night, but the following day fecal vomiting occurred. The patient was now taken to the hospital and laparotomy performed. When the small intestine was drawn out of the abdomen a knuckle of intestine—very red and blue, and thick—was noticed, and deep into the pelvic cavity a knuckle of intestine was strangulated by a thick band of adhesion, which was cut and the intestine returned to the abdomen. The following day the patient had a large bowel movement and made an uninterrupted recovery.

Marcinowski¹ found atropine in full doses valuable for the purpose of relieving pain and constipation in a case of membranous enteritis, and also in a case of incarcerated hernia. In the case of incarcerated hernia the man, aged sixty-two years, after a fall had fecal vomiting and other symptoms of intestinal obstruction, which were relieved by a single injection of 0.005 gramme ($\frac{1}{20}$ gr.) of atropine. Dr. Lüttgen² reports a case of an anæmic woman, aged sixty-five years, who had for several years been afflicted with a slight irreducible femoral hernia and chronic constipation. Being called in to treat her for an attack of constipation

¹ Münchener med. Wochenschrift, October 23, 1900.

² Ibid., November 27, 1900.

more severe than usual, he employed the usual remedies in such cases ; but as the pain, tympany, and nausea increased, after a reasonable delay herniotomy was performed. It was found at the operation that a band of adhesion prevented the return of the intestine into the abdominal cavity. This band was cut, the intestine returned to its normal position, and the patient reacted fairly well from the operation. Upon the morning of the day following the operation fecal vomiting occurred again, and as the enemata for the purpose of moving the bowels were without effect, and the woman's condition was not considered favorable for another operation, he decided to administer 0.005 gramme ($\frac{1}{12}$ gr.) of atropine. The patient showed marked symptoms of atropine intoxication. One-half hour after the atropine injection the patient asked for a bed-pan, but did not succeed in having a stool. After this time the symptoms of atropine poisoning became very marked, and not until six hours later was she sufficiently conscious to respond by voluntary movements when spoken to. During the night, just twelve hours after the injection, she suddenly called for the bed-pan, and had a large bowel movement accompanied by profuse passages of gas, after which she felt much improved. Upon the following afternoon fecal vomiting recommenced, and her general condition became very critical. During the succeeding two days there was no bowel movement, but the vomiting ceased, and the general condition of the patient seemed better. After this time, however, vomiting again returned, the patient lost strength rapidly, and great fear was felt for the outcome. Massage, laxatives, and high rectal injections were tried, but in vain. Another dose of atropine, even in smaller doses, was refused by the patient and her friends, who had been alarmed by the effects of the first dose. The following day (the eleventh day of the acute illness) the patient died. No post-mortem was permitted, but Lüttgen believed that there was no mechanical obstruction, and the symptoms would have been relieved and the patient's life preserved had he been permitted to employ the atropine a second time.

Dr. Demme¹ reports two cases of ileus successfully treated with atropine after the usual remedies in such cases had proved useless. The first was that of a woman, aged twenty-eight years, suffering with fecal vomiting, nausea, abdominal pains, and tympany characteristic of intestinal obstruction. Not having been relieved by the application of the usual remedies for forty-eight hours, she was given subcutaneously 0.003 gramme ($\frac{1}{30}$ gr.) of atropine, after which pain and vomiting ceased, and the patient slept for a few hours. Upon awakening the pain commenced again, and as surgical intervention was refused he gave another

¹ Münchener med. Wochenschrift, November 27, 1900.

hypodermic injection of 0.005 gramme ($\frac{1}{2}$ gr.) of atropine, after which the symptoms progressively subsided, and ten hours after the last hypodermic the patient had a large bowel movement, and recovered without further medication. The second case was that of a man, aged thirty-three years, whose symptoms were practically the same as those of the case stated above. Twenty minutes after the subcutaneous administration of 0.005 gramme ($\frac{1}{2}$ gr.) of atropine the pain ceased, and the patient fell into a quiet sleep for three hours. Six hours later the patient had a large bowel evacuation, and all the symptoms of intestinal obstruction disappeared. Dr. Russow¹ places on record a case of a man, aged fifty years, suffering from marked constipation, nausea, vomiting, abdominal pain, tympany, and other symptoms characteristic of intestinal obstruction. The patient was relieved by full doses of atropine after the usual remedial agents had failed. The obstruction had existed two days prior to his first visit to the patient, and during the next forty-eight hours 0.015 gramme ($\frac{1}{4}$ grain) of atropine was administered. Upon the morning of the third day of his treatment the patient had several large evacuations from the bowels, and all the symptoms of obstruction disappeared. Dr. Proelss² reports a case of intestinal obstruction, with fecal vomiting and collapse, in which he employed extract of belladonna in suppositories, with satisfactory results. After lavage of the stomach, infusion of belladonna in the strength of 1.5 grammes to 100 c.c. of water was given in doses of a tablespoonful every two hours, and suppositories containing 0.20 gramme (3 gr.) each of extract of belladonna were administered by the rectum at the same intervals during the night. The following day the woman showed rather marked symptoms from the use of these large doses, and had several large, thin, bloody evacuations. The symptoms produced by the obstruction immediately subsided, but for fourteen days following the patient suffered from intestinal catarrh. Dr. Proelss believes there was no doubt that obstruction of the intestines was present, that belladonna removed it, and that the patient's condition was such that she would not have withstood laparotomy.

Adam R. Gaehtgens,³ Middeldorf, and V. Polak⁴ each report a case of intestinal obstruction in which relief followed the hypodermic injections of large doses of atropine.

The two cases of Bofinger⁵—one a case of carcinoma of the pylorus and the other a case of incarcerated hernia (neither of which was benefited)—are certainly not cases in which atropine or any other drug could have been expected to act favorably.

¹ Münchener med. Wochenschrift, October 2, 1900.

² Ibid., August 28, 1900.

³ Ibid., April 23, 1901.

⁴ Wiener klin. Wochenschrift, April 25, 1901.

⁵ Münchener med. Wochenschrift, April 23, 1901.

I. L. Van Faudt¹ enthusiastically advocates the use, hypodermically, of atropine sulphate in the algid state of pernicious malaria, for the purpose of overcoming the cyanosis of depression and profuse perspiration. Under $\frac{1}{80}$ grain of atropine sulphate given hypodermically, and in some cases reinforced by strychnine, the whole aspect of the case is changed. He finds that the patients react more promptly and that vomiting and purging cease. Upon theoretical grounds this treatment would appear to be entirely wrong, as the profuse perspiration, purging, and vomiting are the attempts of nature to free the tissues of the extraordinary amount of toxins produced by the malarial organisms, and while atropine might control the symptoms named it would lead to the retention of toxins in the blood.

Arsenic. The epidemic of arsenic poisoning occurring among beer-drinkers in the north of England and the midland counties, from June to the latter part of November, 1900, is the most extensive which has occurred since "the epidemic de Paris," in 1828, in which it is supposed there were 40,000 deaths during a period of four months. During this recent epidemic it is stated that in the city of Manchester alone there were at least 2000 cases, with more than one hundred deaths. During the months of October, November, and December Dr. E. S. Reynolds had under his care at the Manchester Workhouse Infirmary 343 patients, and during November and December, at the Manchester Royal Infirmary, 157 patients, of whom 291 were men and 209 women. Of the 500 cases coming under his supervision there were 13 deaths, 5 of which were men and 8 were women. To Dr. Reynolds belongs the credit of being the first to call attention to this wide-spread epidemic, and also to trace its source to the beer which had been consumed. For twelve months prior to June, 1900, he had been impressed by the unusual number of cases representing various skin eruptions, such as erythema, keratosis, and pigmentation, in the wards of the Manchester Workhouse Infirmary and in the Out-patient Department of the Manchester Royal Infirmary. In June, 1900, during one week, 6 patients who were suffering from pronounced erythromelalgia, and also a number of cases inflicted with herpes zoster, applied for treatment. In August of the same year there were a great many patients admitted to the wards of the Manchester Workhouse Infirmary suffering from what he designates as "alcoholic paralysis." Being unable to satisfactorily account for this sudden and marked increase in the number of persons suffering from these above-mentioned combinations of symptoms—particularly those of the skin—and being unconvinced that these conditions could result from the ingestion of

¹ Merck's Archives, April, 1901.

ethyl-alcohol, and also being cognizant of the fact that arsenic is the only poison capable of giving rise to herpes zoster, he was satisfied that the cases were those of arsenical poisoning and that its source was the beer. About the middle of November he made an analysis of some of the beer most commonly drunk, and by Reinsch's test definitely determined that it was contaminated by arsenic in sufficient quantities to give rise to all of the symptoms that had been observed. The discovery of arsenic in toxic quantities in beer was confirmed by Drs. Delépine and Tattersall,¹ and others, who were able to easily trace the origin to glucose and invert sugar containing large quantities of arsenic. Upon further investigation it was discovered that in the manufacture of the sulphuric acid used in making the glucose and invert sugar, iron pyrites containing large quantities of arsenic had been employed. From 300 samples of beer examined in Liverpool 25 contained only a trace of arsenic; 20 contained small quantities; in 4 there were found $1\frac{1}{2}$ grains of arsenic to the gallon of beer, in 2 $\frac{3}{4}$ grain to the gallon, and in 1 sample $\frac{1}{2}$ grain to the gallon. Dr. Campbell Brown, of Liverpool, analyzed samples of sulphuric acid which had been supplied to the brewers, and found they contained 2 per cent. of arsenic. This sulphuric acid had been supplied to them at the rate of from seven to eight tons a week, and at this rate four tons of arsenic (enough to kill a million people) were supplied in eight months. The symptoms and signs presented by the patients during this epidemic were very characteristic of arsenical poisoning—coryza, œdema, digestive disturbances, pigmentation and lesions of the skin, herpes zoster, and erythromelalgia predominating, and in many cases paræsthesia, hyperæsthesia, pseudolocomotor ataxia, cardiac enfeeblements, and bronchial and laryngeal catarrh. The arsenic was readily revealed in the urine of many patients, and in many cases albumin was found in it.

The treatment found to be most effective was, of course, first the withdrawal of the source of intoxication, the use of moderate doses of digitalis and other cardiac stimulants, the administration of opium for the relief of pain, and the local application of soothing dressings for the relief of irritation.

Dr. Reynolds² strongly advises against the use of potassium iodide, sodium salicylate, antipyrine, phenacetin, and other circulatory depressants. A fact worthy of note is that recovery in many of these cases is extremely slow, the pain and paralysis showing marked tendencies to persist, and in many cases it is believed that the paralysis will be permanent. The sequence of symptoms pointed out by Brouardel and corroborated by Reynolds are as follows: 1. Digestive disturbances.

¹ British Medical Journal, January 12, 1900.

² Lancet, January 19, 1901.

2. Laryngeal catarrh. 3. Disturbances of sensibility. 4. Motor paralysis, pigmentation, and keratosis. As the patient recovers, digestive and bronchial symptoms are first relieved, and the acute skin lesions become chronic. The sensory symptoms may last for months and the motor symptoms for a year or two. In fatal cases death usually results from heart failure.

Reports bearing upon the successful use of arsenic paste in the treatment of epitheliomata are numerous. Drs. Howard Morrow and D. W. Montgomery¹ give the following formula, which they have used in many cases with very satisfactory results :

R.—Acid. arsenosi	5 parts.
Pulv. acaciæ	3 parts.
Cocainæ hydrochloratis	2 parts.

Just before applying the powder, mix with it enough water to make a thick paste. If too little water is used the paste will form into a ball, and cannot be well applied and will not adhere ; if too much water is used it will run.

Dr. O. Lassar, in 1893, reported three cases of epithelioma of the face which had been cured by the administration of the Asiatic pills. In a later² communication he states that there had been no recurrence of the disease, and exhibits photographs to confirm the statement. One of the cases was that of a man, aged seventy-four years, who had taken in all 1000 pills, or a total of 1 gramme of arsenous acid.

Aspirin, or Acetyl Salicylic Acid, is one of the newer synthetic products which is used as a substitute for salicylic acid and the salicylates. The advantage claimed for it is that it does not disorder digestion. It is decomposed in the presence of alkalies, and for this reason should not be prescribed in conjunction with any alkalies or alkaline carbonate. Drs. M. A. Auerbach³ and Nusch⁴ used the drug with good results in the treatment of acute and subacute rheumatism.

Dr. A. Toepfer⁵ employed it not only as an analgesic in acute rheumatism and other rheumatic disturbances, but also found it more or less effective in neuralgia, hemicrania, arthritis deformans, and measles. Vertigo, tinnitus aurium, or headache rarely followed its use.

Dr. P. Zimmermann⁶ employed the drug with satisfactory results in a number of cases of rheumatism. At the beginning of treatment the patient sweated more profusely than when given sodium salicylate, but

¹ Journal of the American Medical Association, March 9, 1901.

² Berliner klin. Wochenschrift, March 11, 1901.

³ Cincinnati Lancet-Clinic, December 15, 1900.

⁴ Munchener med. Wochenschrift, March 15, 1901.

⁵ New York Medical Monatschrift, January, 1900.

⁶ Berliner klin. Wochenschrift, July 2, 1900.

after three or four days, while continuing the remedy, the sweating decreased or almost entirely ceased. No untoward effects were noted from its use.

In seven patients with acute articular rheumatism to whom the drug was administered six were quickly relieved of pain and fever, and recovered rapidly; but in one the fever continued high, and pericarditis developed. One of the patients developed dyspeptic symptoms, which were easily controlled.

Dr. A. Dengel¹ employed aspirin with good results in the treatment of rheumatism, hemicrania, and a severe case of sciatica. The drug has also been used with asserted success in removal of pleural effusions.

The usual dose of aspirin is from 10 to 20 grains (0.60 to 1 gramme) three times a day. It is best prescribed in form of powders or cachets:

R.—Aspirini	3 iv.	gm.	16.00
Pulv. aromat.	3 ss.	gm.	2.00

Pone in cachetas No. xxiv.

Sig.—One or two cachets three times a day.

Bile. Upon a woman with a biliary fistula which entirely prevented the escape of bile into the intestinal tract, Dr. Elliott P. Joslin² was able to study experimentally the influence of bile upon metabolism. He found that when given in daily doses of 30 grammes (5j) dried bile increased the digestion of fats relatively by 50 per cent.; that the digestion of nitrogenous food was improved; that it acted as a cholagogue, and that, while it was not a laxative, the bowels moved satisfactorily during its administration. During the period of the administration of bile, urea and nitrogen were excreted in greater amounts than when bile was withheld; but it was also noted that larger quantities of nitrogen were ingested during the bile period. While taking bile the urine was increased 50 per cent.; but during this period the patient drank several extra glasses of water daily, and therefore the increased diuresis cannot be entirely attributed to the bile. Recent laboratory studies indicate that bile possesses, under certain circumstances, decided antitoxic and bacteriolitic properties; but the subject has not yet assumed a sufficiently scientific or practical basis to make it acceptable for therapeutic application.

Bismuth. In the masterly article by Dr. D. D. Stewart³ upon "Gastric Ulcer: Its Etiology, Symptomatology, and Diagnosis, with Special Reference to Treatment," he takes occasion to condemn the bismuth subnitrate dispensed by most apothecaries as unfit for local use. He says that it is important to know that very few preparations of bismuth,

¹ Berliner klin. Wochenschrift, July 2, 1900.

² Journal of Experimental Medicine, March 25, 1901.

³ Therapeutic Gazette, May, 1901, p. 302.

however pure they may be chemically, are suitable for local use. It is unfortunate that this is not generally understood, as a lack of satisfactory results is often due to this fact. The preparation of bismuth employed must be absolutely free from grit, and its particles so immediately divided that when a small portion is dropped into a vessel of water the bismuth will diffuse itself into a cloud-like form before showing a tendency to settle. We are firmly convinced that the failures in some cases to secure satisfactory results from the use of bismuth subnitrate in catarrhal and inflammatory conditions of the intestinal tract are due to the kind of bismuth used. It should not only be free from grit, finely subdivided, and readily diffusible in water, but should be of such a variety that when applied to mucous membranes it will adhere and form a coating. Many of the varieties of bismuth subnitrates upon the market, while chemically pure and pharmaceutically beautiful, are entirely devoid of this adhesive property, and are therefore almost entirely useless in the treatment of diarrhoea. The adhesive property of bismuth may be easily tested by placing it in a vial with a small quantity of water, shaking it, and then emptying the bottle. The bottle should then be rinsed with water, and if no bismuth adheres to its sides it may be considered unfit for the class of cases mentioned. Another point of some practical bearing in regard to the use of bismuth subnitrate in diarrhoea is, if it passes through the intestinal tract without being changed into black bismuth sulphide, it is entirely without beneficial effects. We believe this to be due to one or two causes: either peristalsis is so rapid that the bismuth is hurried through the intestinal tract before the change can take place, or the intestinal walls are so covered with mucus as to prevent its contact with these.

BISMUTOSE, or BISMUTH ALBUMINATE, is a new compound of bismuth and albumin. It is an odorless, tasteless white powder, gradually changing to a slate-gray color upon exposure to light. It is used in the same doses and in the same class of cases, internally and externally, as are bismuth subnitrate and bismuth subcarbonate, and, like them, is insoluble.

Bromides. When bromides are administered in full and frequent doses over long periods, mental hebetude, gastric indigestion, obstinate constipation, painful acne, perverted metabolism, and other symptoms of bromide intoxication are of common occurrence. Considerable study has been devoted to the best methods of overcoming these untoward effects, and at the same time securing the full medicinal action of bromides. The beneficial results following the temporary withdrawal and the permanent reduction of common table salt from the food of epileptics under treatment with bromides, as suggested by Toulouse,¹

¹ PROGRESSIVE MEDICINE, December, 1900, p. 334.

appears to have stimulated others to carefully study the administration of the much-abused but valuable bromine compounds.

Gilles de la Tourette,¹ in discussing the value of bromides in the treatment of essential epilepsy, asserts that even in patients extremely sensitive to bromide intoxication it is possible to reach and continue adequate doses, without the usual ill effects, if the pupils are carefully watched and the patient kept under surveillance. In patients doing well under bromide treatment the pupils react normally to light and accommodation, and are normally dilated. If the doses are gradually increased there arrives a time when the pupils become dilated and respond slowly to light and accommodation, and the patient feels a slight sensation of physical and mental depression. It is this degree of bromism that Gilles de la Tourette attempts to maintain. If the doses are still further increased the pupils dilate and fail to react, and indicate that the full medicinal dose has been exceeded. He claims that excessive doses are likely to lead to a recurrence of epileptic seizures when they have been prevented by medicinal doses. Should the full medicinal dose be exceeded, as shown by exaggeration of the epileptic symptoms, dilatation of the pupils, or gastric disorders, the bromides are immediately discontinued, the patient is purged, put upon a strict milk diet, and given squills and digitalis for three or four days.

A formula found to be most effective by him is as follows :

R.—Potassii bromidi	3 x.	gm.	40.00
Sodii bromidi	3 iij.	gm.	12.00
Ammonii bromidi	3 iij.	gm.	12.00
Sodii benzoatis	3 iij.	gm.	12.00
Aquæ destillatæ	Oij.	c.c.	1000.00

Misce. Sig.—As a beginning dose take one tablespoonful after breakfast and at bedtime. (Each tablespoonful represents 1 gm. (15 grs.) of bromide. If a seizure occurs at a regular hour it is best to give two-thirds of the daily dose just before the time of the expected convulsion.)

Dr. L. Pearce Clark² considers bromides the drug par excellence for the prevention of epileptic seizures in young epileptics, to secure a possible entire suppression of attacks and ultimate cure of the disease, and, in adults, an amelioration of frequent paroxysms and comparative physical and mental comfort. To secure the best results in all cases receiving bromides, every possible means must be taken to prevent bromide intoxication. The organism must be kept in the highest functional state. In suitable cases prolonged hot baths should be given twice a week on retiring, and each morning upon arising the patient should be given a cold shower-bath and a friction rub. The bowels

¹ Semaine Médicale, October, 1900.

² Buffalo Medical Journal, February, 1901; Medical Record, January 12, 1901; Indiana Medical Journal, March, 1901.

should be regularly moved, the mouth kept clean, the diet modified so as to eliminate or reduce the usual quantity of sodium chloride taken with the food. One of the best ways of eliminating salt from the food is to place the patient on a modified diet of which milk constitutes a large part. He considers hot and cold baths, massage, alimentary antiseptics, high enemata, and all remedial agents designed to improve the patient's general nutrition as absolutely essential to successful bromide medication. If the face shows symptoms of bromide intoxication during the continuance of high doses he advises the application of cloths, wrung out in hot water, to the face for fifteen or twenty minutes each night, the best moist application being a hot saturated solution of boric acid, followed by an application of zinc ointment. The following formula, containing 1 gramme (15 grains) of bromide in each drachm, he finds palatable and convenient :

R.—Potassii bromidi	3 iv.	gm.	15.00
Ammonii bromidi	3 iv.	gm.	15.00
Sodii bromidi	3 iv.	gm.	15.00
Elixir aromatici	q. s. ad 3 vj.	c.c.	180.00

Misce. Sig.—One drachm daily at beginning of treatment.

After a week the doses are gradually increased until the attacks cease. The medicine and hygienic treatment must be continued for a long period. In some cases where the bromides could not be tolerated he found that emulsions of bromine in oil could be substituted with gratifying results. The following formulæ are suggested :

(Ten per cent. bromine.)			
R.—Olei sesami	f 3 ix.	cc.	270.00
Bromi (pure)	f 3 j.	c.c.	30.00
Misce. Sig.—A tablespoonful night and morning, increased as directed.			
R.—Olei sesami	f 3 viij.	c.c.	240.00
Acaciæ (gran.)	3 ij.	gm.	60.00
Syrupi	3 ij.	c.c.	60.00
Olei gaultheriæ	M lx.	c.c.	2.5
Aquæ destillatæ	f 3 vj.	c.c.	180 00

Misce et fiat emulsio et adde bromi gr. dccclx.

Sig.—Tablespoonful night and morning; increase as directed.

Emulsion of bromine modified.

R.—Acaciæ (pulv.)	3 ij.	gm.	60.00
Olei sesami vel olei morrhuæ	f 3 viij.	c.c.	240.00
Aquæ destillatæ	f 3 vj.	c.c.	180.00
Olei gaultheriæ	M lx.	c.c.	2.5

Fiant emulsio et adde bromi gr. dccclx; potassii bromide gr. cccclxxx; bromi gr. xxx; potassii bromidi gr. xv.

Sig.—A tablespoonful night and morning; increase as directed.

Dr. Daniel R. Brower¹ believes that when bromides are being administered in full doses their exhibition in large quantities of alkalinized

¹ Journal of the American Medical Association, May 11, 1901, p. 1341.

water, with moderate doses of solution of sodium arsenate, limits or modifies the acne eruption.

Dr. Elbert Wing¹ reports a case in which death from pneumonia followed the administration of enormous doses of sodium bromide according to the method of Dr. Neil MacLeod,² for the cure of the opium habit.

The treatment of epilepsy by opium and bromides has not met with any very general adoption. The underlying principles of this treatment, as pursued in a series of cases reported by Meyer and Wickel,³ consisted in the administration of $\frac{3}{4}$ grain (40 milligrammes) of powdered opium twice a day for three days at the beginning of treatment, increasing $\frac{1}{8}$ grain (10 milligrammes) on the fourth day, $\frac{1}{6}$ grain (10 milligrammes) on the fifth day, and thus gradually increased until, upon the fifty-first day, the daily dose reached 14 grains (0.9 gramme) of opium. This large dose is given but one day, the opium thereafter being entirely replaced by bromides. A solution in which each dose contains 15 grains (1 gramme) of ammonium bromide and $7\frac{1}{2}$ grains (0.5 gramme) each of potassium and sodium bromide is given three times a day for two days. The dose of combined bromides is then raised to 35 grains (2.1 grammes) for two days, then 40 grains (2.5 grammes) for two days, and finally 45 grains (3 grammes) three times a day. From the very beginning of treatment a tablespoonful of hydrochloric acid solution (1.5 to 200) is administered twice daily after meals. The diet is regulated and modified; coffee, tea, alcohol, bouillon, sausage, highly seasoned articles of food, pepper, mustard, vinegar are forbidden, and salt is restricted. The bowels are kept regular by high enemata and abdominal massage, but no purgatives are used. Upon the first day of the opium treatment a cool bath at 86° F. is given for ten minutes in the evening before eating, and thereafter at the same time daily, the temperature being reduced 2.25° F. and the time one minute less each day, until finally the temperature of the bath is reduced to 70° F. and the duration three minutes. At this temperature and duration the baths are continued for a week, then the duration of the bath at the same temperature is lengthened to four minutes daily for a week, then to five, and finally to six minutes. When the opium is discontinued and bromides substituted the baths are interdicted for a week, then begun again at 86° F. for ten minutes, and then again modified in temperature and time as described above. Marked impairment of nutrition and cardiac weakness are the most important contraindications for the treatment.

¹ Journal of the American Medical Association, December 15, 1901, p. 1571.

² PROGRESSIVE MEDICINE, December, 1900, p. 334.

³ Berliner klin. Wochenschrift, 1900, No. 48, p. 1085.

The number of seizures are not expected to decrease during the opium treatment—in fact, they sometimes increase in frequency—but after the bromides have been commenced seizures are said to become less frequent and violent, and in many cases cease, and the mental state of the patient shows marked improvement. The treatment should continue for a long period after epileptic attacks have ceased, and the patient should be required to lead a quiet life, avoiding physical and mental excesses, excitement, and overindulgence of every kind.

Calmette's Antivenomous Serum. In discussing the value of this serum about a year ago, attention was called to the method employed by Calmette in its manufacture.¹ Recently Dr. Joseph McFarland² details his studies in the production of the serum by immunizing horses with heated and unheated venom, and concludes that the method employed by Calmette, of immunizing with the modified (heated) venom, was the most satisfactory. Dr. W. Hana³ reports the case of a man who (while assisting in the abstraction of poison of a full-sized cobra) was bitten on the thumb, and to whom, twenty or thirty minutes afterward, 18 centigrammes of serum were administered hypodermically. About two and one-half hours afterward the man developed slight stupor, nausea, and some paralysis of the leg. One hour after this time he was given another injection of 10 centigrammes, and in a short while the general symptoms disappeared, although the pain and swelling persisted, and later there was sloughing.

George Lamb and William Hana,⁴ in concluding an article upon the standardization of Calmette's serum, emphasize the fact that at least from 30 to 35 centigrammes of fresh serum should be injected in every case of cobra poisoning. From their experiments they determined that the serum undergoes deterioration in hot climates. Joseph McFarland⁵ believes that the most valuable treatment for the bite of poisonous snakes is the antivenomous serum, which should be given immediately, in doses of from 10 to 20 centigrammes, and repeated at frequent intervals, as required. In addition, the circulation in the region of the bite should immediately be interrupted, so as to prevent absorption of the poison, the fang wound should be at once freely incised, and forcible suction made to extract the poison. From 3 to 6 drops of a fresh watery solution of 10 per cent. calcium chloride should be injected into and about the wound in a dozen different areas, and strychnine should be given hypodermically to stimulate the respiration. He believes potassium permanganate to be of little value.

¹ PROGRESSIVE MEDICINE, December, 1900, p. 327.

² Proceedings of Philadelphia Pathological Society, June, 1901.

³ Lancet, January 5, 1901.

⁴ Lancet, June 15, 1901.

⁵ International Medical Magazine, September, 1900.

Camphor-oxol. This is a liquid containing camphor dissolved in alcohol and hydrogen peroxide. It has been employed as a cleansing and antiseptic application in the treatment of diseases of the ear and nose. Dr. C. F. Holtz,¹ after a limited use of camphor-oxol in otological troubles, considers it a valuable addition to his list of local remedies. Being a non-irritant, it may be used in the early stages of infectious otitis, which may frequently be arrested and complications prevented. Aside from its usefulness in affections within the tympanic cavity, he considers it serviceable in after-treatment of mastoid affections and infections of the external meatus. The solution may be used in full strength, or diluted with sterilized water.

Carbolic Acid. Abundant evidence is at hand to show that strong liquefied carbolic acid, 96 per cent., is a valuable local antiseptic for infected wounds. Owing to the fact that the tissues are coagulated thereby, there is little danger from absorption of the acid, even when used in considerable quantities for swabbing out abscesses or other infected cavities. Any excess of acid remaining may be readily neutralized and removed by thoroughly washing with 96 per cent. alcohol. Dr. Seneca D. Powell² and Dr. von Bruns,³ of Tübingen, Germany, are strong advocates of carbolic acid for wound disinfection. Both have used the acid (according to his own method), and neither has ever seen any ill effects resulting from its use. Dr. Otto L. Muench⁴ testifies to the value of a local application of the liquefied acid for relieving the pain from burns and scalds, and to its freedom from ill effects in these cases.

Zagato⁵ and A. Balduzzi⁶ have successfully employed injections of weak solutions for the relief of pain in acute cases of articular rheumatism. Zagato's case was that of a young man suffering from acute rheumatism, particularly affecting the right knee and foot. As the usual treatment employed did not relieve the intense pain, on the tenth day of the disease he introduced a long hypodermic needle several times into the joint, and withdrew about 60 c.c. of clear synovial fluid. He then injected a 2 per cent. solution of carbolic acid into the joint, and the pain ceased almost immediately; and after three or four days the patient was able to move the joint without suffering. Several days later the left knee became similarly affected, and the same treatment was pursued with equally good results. In Balduzzi's case 1 c.c. of a 3 per cent. solution of carbolic acid was injected into a painful swollen

¹ *Annals of Otolaryngology, Rhinology, and Laryngology*, February, 1901.

² *Journal of the American Medical Association*, December 8, 1900.

³ *Abstract, Philadelphia Medical Journal*, May 18, 1901.

⁴ *Medical News*, August 24, 1901.

⁵ *Gaz. degli Osp.*, Feb. 10, 1901.

⁶ *Ibid.*, April 21, 1901.

joint, with the result that the pain quickly ceased and the inflammation subsided. Dr. J. F. Schamberg¹ calls attention to the fact that the value of carbolic acid as a topical application has so far eclipsed its reputation as a constitutional remedy that many physicians are probably unaware that it has any internal use in dermatology. It is especially valuable in the treatment of psoriasis and pruritus. He quotes Dr. McCall Anderson as recommending it as useful in chronic psoriasis where the patches are not much infiltrated. In this disease it may be given in doses of from 3 to 10 grains daily for a number of weeks, although Kaposi holds that large doses are unnecessary. Schamberg had an opportunity of studying the effects of carbolic acid in several cases of general itching which had lasted for a period of months. In all of these cases there was improvement, and one or two patients were practically cured. Schamberg is not certain as to the way in which the acid relieves the itching. The result is probably brought about (in cases of pruritus due to auto-intoxication) by the internal antiseptic action of the drug, or possibly through the local anæsthetic action of the carbolates, eliminated by the sweat glands. The following formula was found by him to be an agreeable method of administration :

R.—Acidi carbolic.	. . .	℥xxiv vel ℥xxij	gm. 1.50	vel	4.72
Glycerini.	. . .	℥zj vel ℥zij	gm. 4.00	vel	8.00
Vini xerici	. . .	q. s. ad ℥iij			gm. 90.00
Misce.	Sig.—One drachm in water after meals.				

Dr. S. Henry Dessau² believes that in carbolic acid we have a valuable and reliable internal remedy for the treatment of certain diseases of "germ origin." His experience with the remedy extends over a period of six years, during which time he has given it to more than three thousand patients of all ages. The doses employed by him range from $\frac{3}{8}$ grain to 12 grains every two hours, and he insists that the medicine should always be given in solution. He believes that the preconceived ideas as to the highly poisonous action of the carbolic acid are false and misleading, and the prejudices against its internal administration are without foundation. He presents an array of cases and facts to support his views as to the value of the remedy and its freedom from injurious effects when given in very full doses. The diseased conditions in which the drug has been used are puerperal and surgical sepsis, erysipelas, diphtheria, scarlet fever, summer diarrhœa, gastric fermentation, typhoid fever, and he especially recommends it in the protean form of influenza as observed in children. In the more severe cases of influenza accompanied by high fever, general malaise, and extensive catarrhal involvement of the upper air passages, the most

¹ Therapeutic Gazette, June 15, 1901.

² Therapeutic Monthly, May, 1901.

brilliant results were obtained. Even where a pneumonic process had begun, the entire condition was speedily improved by the administration of the acid. He holds that the acid does not disturb or depress the cardiac function in either children or adults, not even when administered to the latter in 12-grain doses every two hours, nor has he ever witnessed any convincing harmful action of the drug on the kidneys. On the contrary, he does not hesitate to employ it (in conjunction with other remedies) in cases of influenza in children complicated by nephritis. Attention is called to the paper of Dr. Wigglesworth, in the *Lancet*, April 3, 1899, in which the internal administration of carbolic acid is not only recommended as a cure, but as a preventive modifier of a contagious disease, such as scarlatina. As much of the carbolic acid on the market contains impurities, such as cresylic acid, rosaic acid, and rosalin, which produce poisonous effects, he insists that only chemically pure acid should be employed, and expresses a preference for Calvert's No. 1 acid. Since 1899, besides the 1 per cent. and 2 per cent. solutions which he continues to give to infants under two years old, he employs a 3 per cent. or 5 per cent. solution in drachm doses, every two hours, for older children, and dessert- and tablespoonful doses of a 5 per cent. solution every two hours for adults. Occasionally, slight, temporary vertigo is experienced after the acid is taken, and in some persons vomiting results; but in adults he considers a dose of 12 grains (well diluted) every two hours entirely harmless.

A convenient formula for a child under two years is as follows :

(One per cent. solution of carbolic acid.)

R.—Acidi carbolici (Calvert's No. 1)	. . . gr. xv.	gm.	1.00
Glycerini ʒ iij.	gm.	12.00
Aqua destillatæ q.s. f ʒ iij.	gm.	100.00

Misce. Sig.—Teaspoonful in water every two hours.

The following formula, to be used in conjunction with the 1 per cent. solution of carbolic acid, is suggested by Dr. Dessau for infants with influenza characterized by a catarrhal condition of the air passages :

R.—Liquor ammonii acetatis	f ʒ iv.	c.c.	16.00
Spiritus ætheris nitrosi	f ʒ j.	c.c.	4.00
Syrupus ipecacuanhæ	f ʒ j.	c.c.	4.00
Syrupus senegæ	f ʒ j.	c.c.	4.00
Syrupus limonis	f ʒ j.	c.c.	30.00

Misce. Sig.—A teaspoonful every two hours.

The value of alcohol for preventing the caustic effects of carbolic acid upon the tissues is well known, and it is a matter of general belief that alcohol is a valuable antidote in cases of poisoning from the ingestion of carbolic acid. With the intention of determining whether alcohol could be used as an efficient antidote in poisoning from the administra-

tion of carbolic acid in toxic doses, and in view of the fact that Dr. Dessau in his paper reiterates the often repeated assertion that alcohol is an efficient physiological antidote against carbolic acid, and as several cases of carbolic-acid poisoning had been reported in which alcohol had been employed, a series of experiments were carried out in the Laboratory of Therapeutics at the Jefferson Medical College. The result of these experiments seems to indicate that it is entirely useless, and probably increases the rapidity of poisoning in such cases. To the first dog experimented upon $2\frac{1}{2}$ drachms of carbolic acid mixed with 4 ounces of 95 per cent. alcohol were given, and in two minutes all the symptoms of carbolic-acid poisoning were marked. Within three-quarters of an hour 2 ounces more of alcohol were administered, and after fifteen minutes this was rejected by vomiting. The animal died in four hours from the time the carbolic acid was administered, without showing any improvement. To the second dog 4 drachms of carbolic acid mixed with oil were given and all the symptoms of poisoning were marked at the end of two minutes. Four drachms of alcohol were now administered, and an attempt was made to wash out the stomach, but, owing to the fact of the animal having been fed, the tube became blocked, and it was impossible to empty the viscus. The animal died within twenty-five minutes after the administration of the carbolic acid without showing any improvement from the alcohol. To the third dog 1 drachm of carbolic acid, 95 per cent., was given, and in five minutes there were pronounced symptoms of poisoning. At this time 2 ounces of alcohol were given, and after five minutes—there being no improvement in the condition of the animal—4 ounces more of alcohol were administered. The animal died in six hours. To the fourth dog 1 drachm of liquefied carbolic acid was administered, and in four minutes all the symptoms of carbolic-acid poisoning had developed. Nine ounces of alcohol were given, and the dog died in one hour without having shown any improvement. To the fifth dog, which had not received any food for twenty-four hours, 2 drachms of a liquefied solution of carbolic acid were given, and after five minutes pronounced symptoms of poisoning were present.

Four ounces of alcohol were now administered, and after fifteen minutes (there being no signs of improvement) four ounces more of alcohol were given, and the whole siphoned off. Immediately after this another 4 ounces of alcohol were given, and the animal vomited freely. Respiration and circulation began at once to fail, and the dog was dead one hour after the administration of the first dose of carbolic acid. The stomachs of all these animals were examined after death, and none of them showed any decided corrosive effects of carbolic acid on the mucous membranes. These series of experiments show that in dogs, alcohol prevents the usual corroding effects of carbolic acid on the stomach ;

that the onset of poisonous symptoms is very rapid if the carbolic acid is mixed with alcohol or oil, and that alcohol in no way modifies, prevents, or controls the toxic effects produced by the absorption of carbolic acid. I am convinced that when 98 per cent. alcohol and carbolic acid are mixed no chemical changes occur, as the following simple tests appear to indicate :

Carbolic acid added to a solution of ferric chloride gives a violet color ; with mixtures of strong alcohol or carbolic acid this color reaction is not developed ; if water is now added to a mixture of carbolic acid, alcohol, and ferric chloride, the color test immediately appears ; carbolic acid added to bromine water gives a white precipitate ; if bromine water in small quantities is added to a solution of alcohol and carbolic acid no white precipitate occurs ; if water is added to a solution of alcohol, carbolic acid, and bromine water, a white precipitate occurs immediately.

Chaulmoogra, or Chaulmugra Oil, is expressed from the seed of *cynocardia adorata*, a tree of the East Indies, and is said to owe its properties to gynocardic acid. When injected subcutaneously it gives rise to an elevation of temperature and a reaction somewhat analogous to that seen after the injection of tuberculin or cantharidin. The oil has heretofore enjoyed some reputation in the treatment of leprosy, and the recent articles of W. Donitz¹ and Hallopeau² show that it is of value in some cases. In the first case treated by Donitz the patient was given a sulphur bath in addition to the chaulmugra oil, and there was marked improvement, but he was unable to determine which of the two remedies brought about this result. When a second case presented itself for treatment, the oil alone was given and with marked benefit. There was a gradual reduction in the size of the nodules, but the most striking effect was seen in the eyes. When the patient was first seen there was marked pannus, and he was practically blind in one eye. At the end of the treatment such improvement had taken place that light could enter into the pupil. To this patient, from one and a half to three grains (0.10, 0.20 gramme) were given subcutaneously at intervals of from ten to fourteen days. Hallopeau states that he had personally witnessed a number of cases in which improvement had been so marked as to practically amount to a cure ; that there is now in the St. Louis Museum, in Paris, a cast taken of a case of leprosy that was considered so typical as to be worth preserving. By the use of oil the patient's condition had improved so much as to enable him to resume his usual life, and no one would ever suspect that he had been a leper. He also

¹ Berliner klin. Wochenschrift, September 3, 1900.

² Bull. de l'Acad. de Méd., March 5, 1901.

cites another case that was exhibited at the International Medical Congress in Paris, in which a permanent cure had been apparently effected by the use of the oil. Patients suffering from ulcerated forms of the disease appear to react more favorably to this treatment than those with the nervous variety. Hallopeau states that the injections are not particularly painful, and that a swelling at the point of puncture disappeared within twenty-four hours, and that, while he favors this method of administration, he has observed good results following the internal use of the oil. Du Castel's experience with the oil was not so favorable. He states that injections of oil were quite painful, and that there were frequently inflammatory infiltrations surrounding the seat of the puncture. In one case the injection induced fatty embolism of the lungs, and in another a tendency to syncope.

Chloralose is a combination of chloral and glucose, appearing in fine, colorless needles, which are soluble in 170 parts of cold water, and freely soluble in alcohol. It is considered by some a more safe and reliable hypnotic than chloral. Its maximum dose for adults is 5 grains (0.3 gramme), which should not be repeated more than once or twice, and at intervals of not more than two or three hours. Dr. James Tyson¹ reports nine cases in which he employed the drug and in which he was well pleased, and thinks it deserving of more general use. A review of his paper leaves the impression that while the drug in most cases acts as a prompt sleep producer if given in high doses, it not infrequently gives rise to symptoms which are, to say the least, alarming. In one case, on two successive nights after doses of 10 grains (0.6 gramme), the patient got up and undressed himself during his sleep. In another case the patient took 5 grains (0.3 gramme) at bedtime for two successive nights and slept well, but upon the third night, as 5 grains did not produce sleep, the patient repeated the dose. The following morning he was found to be in a deep sleep, breathing stertorously, from which his wife could not arouse him. The household became alarmed, but later he awoke feeling well and unaware that anything unusual had occurred. In a third case 10-grain (0.6 gramme) doses had been ordered, and as the effects had not been satisfactory upon a previous occasion, the patient, himself a physician, after an hour repeated the dose. Soon thereafter he fell into a quiet sleep, but later because so restless and unmanageably violent that it was with the greatest difficulty and physical exertion he could be restrained. This condition lasted for four or five hours, but later the patient fell into a quiet sleep from which he awoke feeling well. These were the first cases in which the drug was employed, and where as much as 10 grains (0.6 gramme) were given. In

¹ Journal of the American Medical Association, April 6, 1901.

a later series in which doses of from 2 (0.13 gramme) to 5 grains (0.3 gramme) were given, the results were mostly satisfactory and there were no untoward effects. The following formulæ are suggested as convenient methods of administration :

R.—Chloralose	3 ss.	gm.	2.00
Vini xerici	℥ iij.	c.c.	90.00

Misce. (Shake well.)

Sig.—Tablespoonful at bedtime.

R.—Chloralose	3 ss.	gm.	2.00
Fiat. tabellæ No. vi.			

Sig.—One tablet at bedtime.

R.—Chloralose	3 ss.	gm.	2.00
Elixir. aromatici	℥ iij.	c.c.	90.00

Misce. (Shake.)

Sig.—Tablespoonful in water at bedtime.

Chloretone. Although this new hypnotic has been quite extensively employed during the past few years, we have heard of no convincing statements which deny its being, in suitable cases, one of our most efficient and safe sleep-producing drugs. Dr. A. A. Stevens¹ has used the drug with satisfactory results in a number of cases of insomnia unassociated with organic disease. The best results from its administration were obtained in insomnia accompanying neurasthenia, chronic heart and kidney affection, and during convalescence from acute diseases. Its effects were less satisfactory in cases of delirium tremens, and he does not approve of its use in cases of insomnia due to pain, or in fever where the temperature is over 102° or 103° F. One of its chief advantages over other hypnotics is its freedom from unpleasant after-effects. It seems to have little effect upon the circulation. Even in chronic heart diseases there were no evidences of cardiac depression. He found that it often lost its power to induce sleep after it had been used successively a number of nights. He never employed the drug in doses exceeding 30 grains (2 grammes). Dr. L. I. Hirschmann² strongly advocates the use of chloretone to prevent nausea and vomiting during and after chloroform and ether anæsthesia. To women, and boys not over sixteen, he suggests that about thirty minutes before beginning the anæsthetic, from 10 to 15 grains (0.6 to 1.00 gramme) of chloretone should be taken dry upon the tongue, and washed down with an ounce or two of warm water. During a period of about three weeks, while studying the effects of the drug, he was able to observe its action upon thirty anæsthetized persons, and also to note the condition of thirty other cases in which chloretone was not given. He states that the operators were the same, and the anæsthetic was administered by himself in almost all of the cases, and the operations were of the same

¹ New York Medical Journal, February 23, 1901.

² Ibid., December 15, 1901.

class. In the cases receiving chloretone the amount of anæsthetic required was from one-third to one-half less than those not receiving it, and in none of the cases where the drug was given was stimulation required during anæsthesia. Of the thirty cases given chloretone none were nauseated during the continuance of the anæsthetic, and only three vomited afterward. Of the thirty persons not receiving chloretone twenty-eight were nauseated and vomited, and nineteen upon the following day were still unable to take liquid food. Dr. E. Kuder¹ also employed the drug for preventing vomiting after chloroform anæsthesia and after the administration of morphine. Dr. E. Hollingsworth Siter² recommends equal parts of chloretone and boric acid as a dusting powder for painful granular growths. He believes its value in these cases is limited to the relief of pain, as it has no specific influence on the progress of the cure. Saturated solutions of chloretone have been employed subcutaneously, as a substitute for cocaine, by Dr. E. P. Rasely³ for the purpose of producing infiltration anæsthesia. It has been noted that the anæsthesia is more prolonged than with cocaine, and there is no after-period of depression or excitation. The conclusions of Dr. E. Impens,⁴ drawn from his experiments upon warm-blooded animals, that chloretone is more toxic than chloral hydrates, are entirely at variance with what has been observed by other experimenters and clinicians. He claims that in medium doses it produces deep narcosis, reduces the total air inspired per minute 70 per cent., the volume of individual respiration 60 per cent., and the frequency of inspirations 40 per cent. He further states that it paralyzes the vasomotor centres and heart muscle, and causes a marked lowering of the temperature to below the normal by increasing heat radiation, and by its paralyzing action upon the cellular protoplasm, as shown by the marasmic condition which remains for a considerable time after waking. Attention is called to the well-known effects of some chlorine compounds to cause fatty degeneration, but he presents no evidences that this condition was produced in any of the animals experimented upon by himself.

The following formulæ are suggested by Dr. Darche:⁵

For painful leg ulcer:

R.—Pulv. amyli	3 ij.	gm.	8.00
Zinci oxidi	3 ij.	gm.	8.00
Mercurolis	gr. xv.	gm.	1.00
Chloretoni	3 ss.	gm.	2.00
Petrolati	3 j.	gm.	30.00

Misce et ft. unguent.

Sig.—To be applied on pieces of lint, constantly re-covering the affected areas.

¹ Kansas City Medical Record, July, 1901. ² Therapeutic Gazette, March 15, 1901.

³ International Journal of Surgery, April, 1901.

⁴ Archives Internationales de Pharmacie, 1901, No. 8.

⁵ Canadian Practitioner and Review, April, 1901.

As a palliative for ulcerated hemorrhoids :

R.—Mercuriolis	gr. v.	gm.	0.30
Chloretoni	gr. xv.	gm.	1.00
Acidi borici	℥ss.	gm.	2.00
Petrolati	℥j.	gm.	30.00

Misce et ft. unguent.

Sig.—To be applied three times daily.

For ulcer of the rectum :

R.—Mercuriolis	gr. j.	gm.	0.065
Chloretoni	gr. ij.	gm.	0.13
Acidi borici	gr. viij.	gm.	0.50
Olei theobromatis	gr. xxx.	gm.	∞.00

Misce et ft. suppos. No. i.

Sig.—To be inserted at bedtime.

Chloralamide. Dr. S. V. Clevenger¹ strongly advises the substitution of chloralamide for chloral hydrate for the larger number of cases in which the latter substance is employed. He considers it a far safer drug than chloral; in fact, no deaths are recorded from its use. It is less irritating to the mucous membrane, and in full medicinal doses does not depress the circulation nor give rise to after effects. The usual dose of chloralamide is from 10 to 15 grains (0.60 to 1.00 gramme), and, as a rule, not more than 60 grains (3.60 grammes) should be given in twenty-four hours. It acts more rapidly when given in solution than in the form of powders or tablets, and is soluble in twenty parts of cold water and one-half part of alcohol. No difficulty should be experienced in prescribing it in liquid form. It should not be dissolved in hot water, nor prescribed in conjunction with alkalies, as it is decomposed by both.

Chromic Acid. Some years ago Dr. J. William White recorded a case of poisoning due to the local application of chromic acid in the treatment of condylomata of the genitals. Dr. John W. Shaw² reports another case of the same kind. In both of these instances the strength of the solution employed was 100 grains of the acid to an ounce of water. In Dr. Shaw's case there were nausea, rapid pulse, cold extremities, sweating, and, in fact, all the symptoms of profound shock. As soon as the toxic symptoms appeared the dressings were immediately removed, but the condition continued for thirty-six hours, after which time the patient slowly returned to the normal state. Dr. H. du Fougeray³ reports three cases of epitheliomata in the pharynx which he had successfully treated by curettement and cauterization with 0.5 per cent. of chromic acid.

Collodion. The employment of collodion as a local application to relieve itching in the treatment of pruritus ani, as suggested by

¹ Medical News, December 8, 1900.

² Virginia Semi-Monthly, February 8, 1901.

³ Annales des maladies de l'oreille, January, 1901.

Dr. G. A. Duncan,¹ is a novel use of this preparation. He says: "Separate as widely as possible the folds of the skin, and then apply common collodion freely." This will relieve for a time all the itching. Dr. Allen F. Haight² suggests the use of collodion in the treatment of exophthalmic goitre. His method is to relax the muscles by placing the patient's head in an easy position, apply a thick coating of collodion over the enlarged gland and promote its rapid evaporation by using twenty or thirty pounds of air-pressure. To keep up the pressure the application should be repeated at intervals of from three to four days. He claims that beneficial results are brought about by the compression, which reduces the size and secretory function of the gland, and diminishes its blood-supply.

Creosote. Some years ago Dr. H. A. Hare called attention to the fact that any of the soluble sulphates were efficient antidotes to creosote. As the latter substance is used internally to a great extent in the treatment of tuberculosis and subacute and chronic inflammations of the upper air passages, and cases of poisoning are liable to be of frequent occurrence, the knowledge of the antidotal property of the soluble sulphates is a matter of practical value. Attention is directed³ to the report of a case by H. M. Hewlett, where a child, after swallowing two drachms of creosote and developing all the dangerous symptoms of poisoning from this drug, was successfully treated by washing the stomach with about two pints of strong solution of magnesium sulphate (of which six ounces were left in the stomach) by the application of extreme heat and the administration of strychnine and brandy.

Digitalis. While there may still reasonably exist some difference of opinion as to the advisability of using digitalis in fatty degeneration of the heart and in aortic regurgitation, much of the discussion as to its value in diseases of the heart is needless, and would cease if its physiological action was more generally understood. Surely, it can no longer be doubted that digitalis in medicinal doses is a stimulant to the heart and its contained ganglia, that it does slow the heart, that the pulse-wave is increased in volume and force, and the arterial tension is raised. Dr. H. A. Hare⁴ has conclusively proven that the drug actually improves the nutrition of the heart. The whole cardiac therapy of digitalis may be stated in a few words. It will not repair damage to the valves of the heart, and can only lead to harmful effects in valvular lesions if the heart is sufficiently strong to sustain a normal circulation. If, on the other hand, the condition is one in which the heart fails to

¹ American Medical Compendium, February, 1901.

² Chicago Medical Record, March, 1901.

³ Ed. Therapeutic Gazette, March 15, 1901.

⁴ Therapeutic Gazette, December, 1897.

do its proper amount of work, the drug is indicated. In this connection the paper of Dr. William Henry Porter¹ is interesting, though we do not agree with him in some important particulars. He calls attention to the good and bad effects to be obtained from digitalis as a therapeutic agent, and clearly shows that the contradictory statements regarding the value of the drug in cardiac and renal affections are due, not only to the complex composition of its glucosides and to the lack of uniformity in the strength of the preparations, but in many instances to an imperfect knowledge of the pathology of the disease in which it is given, and of the physiological action of the drug. The only cardiac lesion in which he believes it should be employed is in stenosis or in insufficiency of the left auriculo-ventricular orifice, accompanied by lowered arterial tension and venous engorgement, and in these conditions it is of value for only a few days. As soon as this is overcome its administration should be suspended. When the normal tension has been reached and passed the action of digitalis is detrimental to all the physiological functions of the body, because it increases the work of the cardiac muscle, "poisons the muscular fibres, and by abnormally contracting all the arterioles, progressively decreases the nutritive supply to the organs." He advises against its use in all aortic lesions, in fatty degeneration or in "any enfeebled condition of the heart muscle." He does not believe that the poisonous symptoms sometimes attributed to the cumulative action of digitalis can be due to the storing up in the system of any of its glucosides, which are later suddenly eliminated into the circulation in large quantities and give rise to toxic effects. He believes that the weight of evidence goes to prove that the active principles of the drug are rapidly decomposed in the system into carbon dioxide and water, with the production of heat, and that they are never found in their original forms in the excretions of the body; also, that the so-called cumulative effects are brought about by a combination of three factors, by augmenting the work of the heart, by poisoning the heart muscle, and by its vaso-constricting influence upon the coronary arteries, thereby lessening the nutrition of this organ. We have already expressed an opinion as to the action of the drug on the muscular fibre of the heart and its nutritive power over this organ, and are inclined to agree that ordinarily the glucosides do not accumulate in the tissues. There are, however, two diseased conditions where it does appear that the toxic effects can be accounted for in no other way than by the retention of the active principles in the tissues, and their sudden elimination when these conditions cease to exist. For instance, digitalis given to a patient with high fever (even repeated doses) exerts no effect;

¹ American Medicine, April 20 and 27, 1897.

but if the temperature is reduced by cold baths, antipyrine, or any means, the drug previously given often suddenly acts so violently as to produce poisoning. This same effect is noted in persons suffering with ascites. If digitalis has been administered to the patient for a considerable time, and tapping has been resorted to, sudden and often alarming symptoms of poisoning are apt to appear as soon as the fluid is withdrawn and pressure upon the large vessels thereby relieved. Taking up that part of Porter's paper referring to the short period only in which digitalis is useful, we believe that, generally speaking, he is correct, but in many cases of weak heart, while we are able to secure satisfactory results by rest, massage, baths, gymnastics, or modification of diet, with occasional recourse to medicine, there comes a time when we can no longer procure lasting compensation without the continuous use of some one of the cardiac stimulants. In such cases digitalis is usually our most helpful drug; if necessary, there can be readily substituted, for a time at least, strophanthus, cactus, adonidin, or caffeine. As a diuretic, Porter believes that when used guardedly, in properly selected cases, digitalis possesses great power for good, but applied without a perfect knowledge of its limitations, it is capable of doing harm. He asserts that when digitalis is given to the normal individual in medicinal amounts, while it raises the general blood-pressure, owing to the fact of there being no obstruction to the exit of blood from the kidney, the hydraulic pressure in the glomerule is not increased, but that the speed of the blood through the kidney is increased. As the pressure in the glomerule is not raised above the normal, the amount of urine excreted is not increased, while the rapidity of the flow does not permit of sufficient time for the epithelial cells to take up and fully oxidize and eliminate the nitrogenous excretions of the body. If still larger doses of digitalis are given to the normal individual (or to those suffering from some renal lesions), so as to bring the system more completely under the influence of the drug, the renal artery may become so contracted as to decrease the elimination of water, diminish the nitrogenous excretions, and lessen the perfection in the nutritive exchange between the blood and the tissues of the kidney. In those lesions of the kidney where the venous exit by way of the large veins of the organ is not impeded, digitalis drives the blood through the organ more rapidly without increasing the hydraulic pressure in the glomerule, and, therefore, does not act as a diuretic, but, on the contrary, decreases the excretory function and impairs the nutrition of the organ, and thereby makes the kidney lesion worse. Upon the other hand, in lesions of the kidney characterized by low arterial tension with venous engorgement and obstruction to the exit of blood from the kidney, digitalis increases the excretory function of the organ and improves its nutritive condition.

From a review of the paper of Dr. Harry Orville Hall,¹ we infer that he is of the opinion that digitalis frequently gives rise to hallucinations and delirium, and that not infrequently these nervous symptoms are attributed by physicians to the disease instead of to the drug.

S. Solis Cohen² testifies to the value of full doses of digitalis in reducing the fever and quieting the pulse in the latter stages of chronic pulmonary tuberculosis and in recurring acute attacks of tuberculous bronchopneumonia or of lobar pneumonia in tuberculous patients. The best results are to be obtained only when the drug is given continuously and fearlessly up to the point of tolerance. He expresses a preference for Merck's digitalin, to be given in doses of $\frac{1}{24}$ to $\frac{1}{8}$ of a grain—or even more—twice a day.

Diphtheria Antitoxin. To the great number of physicians who have employed antitoxin in their hospital and private practice, and to those who have kept posted upon the overwhelming number of reports of brilliant successes obtained from the use of this agent in the treatment of diphtheria, it would seem like dwelling on ancient history to continue to praise this valuable therapeutic serum. There are some, however, who refuse to be convinced and who still argue against the use of antitoxin in diphtheria. Although the serum has been used hundreds of thousands of times without ill effects, they still contend that it is a dangerous remedy; and though the mortality has been reduced 50 per cent., they attribute this to other causes than the use of the serum. Epidemics have been completely broken up by preventive inoculations, yet they refuse to believe that the antitoxin contributed anything toward the subduing of such outbreaks. As long as there is a doubt in the mind of any physician, we believe that the evidence, which is continuously accumulating, should be presented to him.

One of the most valuable statistical reports upon the use of diphtheria antitoxin is by Otto Jelinck,³ who has tabulated, as far as possible, the published reports of observers in all parts of the world to the close of 1898. The number of cases covered by these reports are 52,785, with 8525 deaths—a death rate of 16.15 per cent. of the whole number; 35,095 cases were treated in hospitals, with a death rate of 18.23 per cent., and in private practice and hospitals there were 19,647 cases, with a death rate of 12.16 per cent. In addition to these cases he adds collective reports from Austria, Hungary, Bosnia, Germany, Russia, and the United States, of 127,359 cases, with the death rate 14.2 per cent. His tables showing the results obtained by the early treatment with antitoxin are interesting. Thus, of the total number

¹ American Medicine, June 29, 1901.

² Journal of the American Medical Association, February 23, 1901.

³ Des (Esterreichische Sanitatswesen, 1900, No. 52.

of 52,521 cases treated with antitoxin there is a death rate of 15.28 per cent. Of these, 5970 were treated with antitoxin upon the first day of the disease, with a death rate of only 5.7 per cent.; 17,088 cases received antitoxin on the second day, with a death rate of 8.49 per cent.; 13,203 cases were injected with it on the third day, with a mortality of 15.56 per cent.; 6744 cases upon the fourth day received the treatment, with a death rate of 23.36 per cent.; 4288 were first treated with antitoxin on the fifth day, with a death rate of 30.2 per cent.; 3313 cases did not receive the treatment until after the fifth day, and the mortality rate was 27.89. In 1965 cases in which it was not specified upon what day antitoxin treatment was begun the death rate was 15.28 per cent. These figures are most convincing, and show the great necessity for prompt treatment if the best results are to be expected. The beneficial results of antitoxin treatment in severe cases of diphtheria with laryngeal stenosis are shown by the paper of Galatti,¹ who reports the results obtained upon 61 carefully studied cases seen during the course of several years. Of the total number, 29 were treated before the day of serum therapy, and 32 after. Of the 29 cases of laryngeal diphtheria under treatment before the introduction of diphtheria antitoxin, 6, or 21 per cent., recovered without operative intervention. Of the 32 cases treated with antitoxin, 14, or 44 per cent., recovered without operation. Of the 29 cases not receiving antitoxin, 23 were intubated, and 11 of these, or 47.8 per cent., died. Of the 32 cases receiving antitoxin, 18 were intubated, and one, or 5.5 per cent., died, and in this one case the quantity of antitoxin was far less than the quantity recommended at the present time. The value of antitoxin is further demonstrated by the fact that in the intubated cases where the antitoxin was employed the tube could be removed earlier than in those cases not receiving it. The results obtained by the use of this valuable agent have been most remarkable, and it is certainly within the bounds of moderation to state that by its use the mortality rate from diphtheria has been reduced 50 per cent. We are learning by experience, however, that this rate might have been and will be further reduced by larger and more frequently repeated injections. The initial dose in each case should be the largest the severity of the case indicates, and be repeated with such frequency and in such quantities as is required in each individual case. This is especially urged by many competent observers who hold that the agent is only capable of good, and that no ill effects can be justly attributed to it. The papers of Dr. John H. McCollom² and Fred Grant Burrows,³ in which they make a plea for

¹ Wiener med. Wochenschrift, 1901, Nos. 2 and 3.

² Boston Medical and Surgical Journal, December 20, 1900.

³ American Journal of the Medical Sciences, February, 1901.

larger doses of antitoxin in the treatment of diphtheria, are most instructive. They strongly urge that in diphtheria the remedy should be administered at the earliest possible moment and in such doses and with such frequency as to produce the characteristic effects of the antitoxin on the diphtheritic membranes. In some cases only 4000 units are required, while in other instances as much as 60,000 or 70,000 units may be necessary to save the life of the patient. Some patients who were almost moribund were saved by the use of antitoxin, while in operative cases the beneficial effects of large doses of antitoxin were most pronounced. In nearly 8000 cases where antitoxin had been employed by McCollom, no injurious effects had followed its use. The rashes which were frequently annoying in many cases where the drug was used never imperilled the life of the patient, and were really of little significance when compared to the good effects obtained from the injections. We occasionally hear the argument that post-diphtheritic paralysis is more frequent now than before antitoxin came into general use. This argument can be met, however, by stating that more of the severe cases recover, and that, though antitoxin has been capable of saving the lives of patients, it does not prevent paralysis that sometimes follows an attack of diphtheria.

During the year 1900, Ch. Talamon¹ treated in the Bichat Hospital 50 cases of pneumonia with antidiphtheritic serum. He states that two or three injections of 20 c.c. are usually sufficient in patients under fifty to fifty-five years of age. An injection is usually followed by a lowering of the morning temperature, and if the temperature rises again in the evening a second injection is given. In all adynamic cases, or in cases not seen before the third day of the disease, he believes they should receive two injections a day. In some severe cases as much as 200 to 260 c.c. of the serum was used during several days, and in none of these cases were there any deleterious results, although in 5 of the 50 cases there was an erythematous eruption and articular pains. Of the 50 cases treated, 48 of whom were addicted to the immoderate use of alcohol, there were but 7 deaths, six of these occurring in patients not seen until the fifth day of the disease. There was but 1 death, that of a woman—seventy-two years of age—out of a total of 25 cases who had received the serum treatment before the fifth day. The mortality rate of pneumonia in the Bichat Hospital in previous years was at least 24 per cent., and in 1899, 37 per cent. Talamon believes that by the prompt and frequent use of antidiphtheritic serum the duration of the disease in many instances may be shortened and the death rate in pneumonia reduced to about 10 per cent.

¹ *Annales de l'Institut Pasteur*, February 28, 1901.

Raynaud¹ and Negel² also testify to the value of diphtheria antitoxin in the treatment of pneumonia.

The use of diphtheria antitoxin in the treatment of scarlet fever and as an immunizing agent in this disease is strongly advocated by Dr. E. H. Dalton,³ who, about two years ago, accidentally discovered that by the use of this serum the attack of scarlet fever was rendered much milder. The favorable results in this case led him to the further use of the remedy, which he states he has used about twenty-five or thirty times without a death. In severe cases he has been impressed by the marked amelioration of all symptoms following the use of the antitoxin.

In two cases of pseudomembranous conjunctivitis, from one of which diphtheria bacilli were obtained in the culture, Schlesinger⁴ employed diphtheria antitoxin with excellent results.

J. N. D'Esterre⁵ used 1500 units of antitoxin with the most satisfactory results in a case of membranous non-diphtheritic tonsillitis.

Ergot. There can be no doubt that ergot is a valuable remedy for preventing and controlling hemorrhage, particularly in uterine bleedings; but lately its value in pulmonary and cerebral bleeding has been called into question, and we believe that it has been conclusively proven to increase rather than diminish hemorrhage in these organs. It will be remembered that its power to control hemorrhage is due to its vaso-constricting influence on the bloodvessels, and as it is devoid of any such effect on the bloodvessels of the brain or lungs, by constricting the bloodvessels of every other part of the body, there is a greater determination of blood to these vessels, and consequently increased hemorrhage. The conditions are different in uterine bleedings. It not only contracts the bloodvessels of the uterus, but by causing tetanic contraction of the muscle fibres of the organ its blood-supply is diminished and hemorrhage controlled. F. A. Seymour⁶ also questions the value of ergot in intestinal hemorrhage. He asserts that he has seen it produce a peristaltic diarrhoea as a result of its action on the muscles of the intestines, and that a protective clot stands a poor chance of adhesion after the use of the drug. It is very probable that in gastric hemorrhage due to ulcer it produces similar results. We have reason to know that many of the preparations of ergot on the market are entirely inert, and as there are no chemical or pharmaceutical tests for determining their value, we believe that preparations made from ergot

¹ *La Médecine Moderne*, March 27, 1901.

² *Ibid.*, May 1, 1901.

³ *St. Louis Medical Review*, April 6, 1901.

⁴ *Münchener med. Wochenschrift*, January 10, 1901.

⁵ *British Medical Journal*, April 6, 1901.

⁶ *Merck's Archiv*, September, 1900.

which has been previously physiologically tested should be the only kind employed.

Ethyl Bromide. The reports of Dr. E. E. Montgomery have caused a more general employment of this anæsthetic in obstetrical and other cases where only a brief period of anæsthesia is required. Wilmer Krusen¹ states that during the past seven years he has used ethyl bromide extensively in obstetrical and gynecological practice, and has never witnessed an accident or alarming symptoms. The drug is unsuited for prolonged operations, and its greatest field of usefulness is during the latter part of the second stage of labor, when it may be administered in such quantities as to relieve the pain without producing unconsciousness or preventing uterine contraction. He also employs the anæsthetic when making bimanual examinations in patients with rigid or tender abdominal walls, and for performing brief surgical operations such as dilatation of the urethra or anus, and evacuations of vaginal and mammary abscesses. In the later cases its method of administration is to pour about a drachm of the drug on a cone-shaped towel or napkin, which is placed over the mouth and nose, with the edges held closely to the face to prevent any air from entering. Under these circumstances narcosis should come on in from thirty to forty seconds, and last from two to three minutes. When unconsciousness is complete the mask should be removed. Attention is called to the fact that certain patients, especially alcoholics, resist the drug, and in these cases the anæsthesia should never be forced. The advantages which he claims for this drug over all other anæsthetics (when only a brief period of anæsthesia is required) is the short space of time necessary to render the patient unconscious, the small quantity of the drug employed, the rapidity of its elimination from the system, the simplicity of its administration, and the comparative freedom from unpleasant sequelæ.

Euphthalmin. It has been frequently stated that glaucoma never results from the instillation of this valuable mydriatic, and it has undoubtedly been employed in hundreds of cases which escaped this accident. Knapp,² however, has reported a case where acute glaucoma followed the use of euphthalmin in the eye. By the administration of pilocarpine, and the instillation of eserine into the eye the tension returned to the normal.

Euchinin, or Euquinin, is an ethyl carbonic ester of quinine. It is a white, crystalline, tasteless substance, made by the action of ethyl carbonyl chloride upon quinine. It is almost entirely insoluble in water, but is soluble in alcohol, ether, and chloroform. Its action is said to

¹ Philadelphia Medical Journal, November 3, 1900.

² Archiv f. Augenheilkunde, Band xlii., Heft 3.

be identical with that of other salts of quinine, but possesses the great advantage of being almost tasteless. Its dose is about the same as that of quinine sulphate. It has been employed in the treatment of malaria, whooping-cough, and other diseases where quinine is of value, and it is said to be less likely to give rise to gastric disturbances and ringing in the ears than other cinchona alkaloids. Albert Bernheim¹ has used the salt in the treatment of malarial fever, neuralgia, and whooping-cough, and finds it as valuable as quinine. Cinchonism and gastric disorders were less frequent than with quinine, and in no case did he see any unpleasant after-effects. A. Celli² does not think the use of quinine a practical prophylactic against malaria. He states that few persons can tolerate the amount required to be effective, but that with euchinin it is possible to accomplish the purpose without any inconveniences. In his extensive experience with the drug he found that in doses of 0.50 gramme ($7\frac{1}{2}$ grains) for adults, and 0.25 gramme (4 grains) for children, taken night and morning, it was an effective prophylactic against malarial infections. Although given in these doses to some persons for a period of five months, he had observed no gastric disorders, ear symptoms, or disturbances of any kind from its use. As euchinin is practically insoluble in water, and almost devoid of taste, it may be best prescribed in the form of powders, although if desired it may be given in a mixture to which some flavoring syrup is added. The following formula suggests a convenient manner for prescribing :

R.—Euchininæ 3j. gm. 4.00

Fiat chartulæ No. xii.

Sig.—One powder night and morning as a prophylactic.

In the treatment of whooping-cough in children the following is a convenient formula :

R.—Euchininæ gr. xxx. gm. 2.00

Theobromatis (chocolate) ʒiv. gm. 16.00

Sacchari ʒiv. gm. 16.00

Pulv. tragacanth. gr. xv. gm. 1.00

Aquæ rosæ q. s.

Misce et fiant trochiscæ No. xxx.

Sig.—One lozenge to be taken every two or three hours.

Formaldehyde. The use of the aqueous solution and of the generated gas as a disinfectant, antiseptic, and deodorizer was fully discussed in these pages about a year ago. Attention was also called at that time to reports bearing on its successful application in the treatment of whooping-cough, hyperidrosis, bromidrosis, night-sweats of phthisis, cutaneous cancers, warts, condylomata, rodent ulcers, and ring-

¹ Merck's Archiv, November, 1900.

² Centralblatt f. Bakt., February 21, 1901.

worm. During the past year there have been numerous reports confirming its value in these conditions, but the subject of greatest interest concerning its use is the treatment of pulmonary tuberculosis by intravenous injections of aqueous solution of the gas. In the Harveian lectures by Dr. Robert Maguire,¹ he expressed the belief that none of the drugs or medicines heretofore employed by the mouth, subcutaneously, or by direct injections into the lungs, had brought about any good results by their effect upon the tubercle bacillus or its cogeners, the staphylococcus pyogenes and pneumococcus. Believing that the lungs could be reached more directly through injections into the venous system, he found mercuric cyanide and potassium iodide too dangerous for use upon human beings, and diastase, cytase, and neucleinic acid too feeble in their effects upon the micro-organisms to be of any practical value; moreover, they caused marked febrile reaction. He then decided to try formaldehyde solution in the strength of 1 in 2000 in normal salt solution, of which 50 c.c. (12 drachms) were injected into a large vein of the arm by means of a specially prepared apparatus. The treatment was employed in fifty cases of advanced pulmonary tuberculosis, and appears to have been encouraging. In all of the cases it was claimed that improvement was noted in the clinical signs; there was diminution in the amount of expectoration, and a disappearance of the tubercle bacilli in the sputum. It is probable that if this method had originated with or been suggested by someone less qualified to speak on the subject of tuberculosis, or less eminent in the medical profession, it would have excited little comment, but coming as a suggestion from Dr. Maguire, the subject has attracted considerable attention.

Dr. E. Viko² calls attention to experiments he claims to have carried out three years ago, with the intention of determining whether the solution of formaldehyde could (without injuring the animal) be injected into a vein in sufficient quantity as to disinfect the lung, and if injected into a vein of the foreleg, the gas, after permeating the lung, would escape by the mouth. Into a vein in the foreleg of a dog he injected 120 minims of formalin (45 minims of pure formaldehyde) mixed with 2 ounces of warm normal salt solution. By holding to the animal's mouth a piece of white blotting-paper saturated with a solution of fuschine and then decolorized with diluted hydrochloric acid, he was able to definitely determine that formaldehyde gas was eliminated with the breath, by noting the change of color of the paper. The animal died in two or three minutes. To a second dog 25 minims of formalin (10 minims of pure formaldehyde) were

¹ British Medical Journal, December 15, 1900.

² Journal of the American Medical Association, February 2, 1901.

administered in the same manner, and to a third dog 37 minims of formalin (15 minims of pure formaldehyde) were given. In the last two animals it was found that the formaldehyde was eliminated with the breath, and they seemed as well after the experiments as before. Arterial blood was heated to determine if it would give off formaldehyde gas, and as the decolorized fuschine paper was not changed to a yellow the blood was thought to be free from it. There have been numerous reports referring to the treatment of tuberculosis by inhalations of air charged with small quantities of formaldehyde gas, but it is highly irritating to the mucous membrane of the air passages, and does not seem to have been of any particular value. Demidoff¹ reports a number of cases of favus in which 0.5 per cent. solution of formaldehyde has been employed with good results.

H. O. Reik² and Nathan G. Ward³ strongly recommend weak solutions of formaldehyde in the treatment of suppurative otitis media. Reik suggests the use of about 1 drachm of a 40 per cent. solution to one pint of boiled water for irrigating the ear night and morning. He does not claim that all cases are cured by this means, but in those susceptible to cure by syringing with an antiseptic fluid, "formaldehyde will accomplish the good result with more certainty and considerably less time than any other antiseptic employed at the present time." In suitable cases Ward advises that after cleansing the ear the head should be inclined to the opposite side and an aqueous solution containing five drops of formaldehyde to the ounce be instilled into the ear with a medicine dropper, enough being used to fill the external auditory canal. The patient is then given a solution of this strength, which he is directed to warm and instil into the ear in quantities of from 5 to 10 drops night and morning. The patient is directed to lie in such a position that the fluid will not escape from the ear for about ten minutes. In acute cases the strength of the solution should be from 1 to 3 drops of formaldehyde to the ounce of water, as stronger solutions produce severe pain. In more obstinate cases, and those with small granulations, the following formula is employed :

R.—Formalin	gtt. v.	c.c.	0.30
Alcohol	℥ij.	c.c.	8.00
Aque	q. s. ad ℥j.	c.c.	30.00

The well-known irritative properties of formaldehyde, even when used in very diluted solutions, have somewhat militated against its use in gargles and mouth-washes. Alfred C. Jordan⁴ makes a suggestion that this difficulty can be obviated to a great extent by using glycerin as a solvent instead of water. Mixtures of from 1 to 4 per cent. of

¹ Merck's Archiv, April, 1901.

² Maryland Medical Journal, January, 1901.

³ American Medicine, June 15, 1901.

⁴ Lancet, February 16, 1901.

formalin in glycerin will keep for several weeks, but it is better to prepare such mixtures fresh when wanted for use. For follicular tonsillitis he believes that a mixture of from 2 per cent., 3 per cent., or 4 per cent. formalin in glycerin is almost a specific. When applied in such cases no drinks should be taken by the patient for half an hour after the treatment. In aphthous stomatitis and thrush he believes that the best treatment that can be carried out is to make an application of a 2 per cent. solution, and thereafter use a mixture of glycerin and boric acid. In ulcerative stomatitis the following formula is suggested :

R.—Formalini	1 part.
Iodii	2 parts.
B. eucainæ	2 parts.
Glycerini	q. s.	100 parts.

In conjunction with the local application of the above prescription he favors the internal administration of potassium chlorate. Cases of acute formaldehyde poisoning are reported by L. Zorn¹ and J. Klueber.² In Klueber's case a man, aged forty-seven years, swallowed by mistake a small quantity of formalin with a large draught of mineral water. He almost immediately developed stupor, followed by coma, which lasted several hours. There was redness of the conjunctiva and pharynx, and anuria persisted for fourteen hours. The urine passed after this time contained formic acid. In Zorn's case the patient was a man, aged forty-four years, who by accident drank an ounce of a solution of 30 to 40 per cent. of formalin. Being aware of his mistake, he immediately took some milk and vomited, and as soon as he reached the hospital his stomach was washed out. The symptoms present in this case were burning in the mouth, pharynx, and stomach, nausea and vomiting, vertigo and dyspnoea. The odor of formalin was present in his breath, his skin was cold, and the lips and extremities were cyanotic. Absolute anuria persisted for twenty-four hours, the bladder remaining empty. The patient did not lose consciousness. The following day he voided a little more than three ounces of urine, which contained albumin, hyaline and granular casts, and leucocytes. The first few days following he had several large, loose, bowel movements, which contained mucus in considerable quantities. The treatment pursued in this case consisted in washing out the stomach, warm baths, mineral water given frequently, and such diet as would be ordinarily given in gastro-enteritis. Dr. Martin H. Fischer,³ before the Chicago Pathological Society, reported the results obtained from a study of the toxic effects of formaldehyde and its aqueous solutions. When inhaled it gives rise to inflammatory changes throughout the respiratory tract. When introduced into the stomach it produces

¹ Münchener med. Wochenschrift, November 13, 1900.

² Ibid., October 9, 1900.

³ Journal of the American Medical Association, March 2, 1901.

dyspnœa, depression of temperature, tachycardia, weak pulse, vomiting, and gastritis (characterized by intense congestion), necrosis, and leucocytic infiltration of the gastric mucous membrane. Intraperitoneal injections of a strong solution produce fibrohemorrhagic peritonitis of varying intensity, according to the strength of the solution; while intraperitoneal injections of small quantities of a diluted solution of formalin induce a chronic peritonitis with great connective-tissue proliferation, and a striking eosinophilia. Subcutaneous injections of formalin produce marked exudation and leucocytic infiltration. The injection of formalin into the conjunctival sac is followed by iritis, a single drop of the concentrated solution being sufficient to permanently injure the eye. He stated that in whatever way formalin was introduced into the body, certain systemic changes resulted. In addition to the leucocytic infiltration which follows, it gives rise to degenerative changes and focal necrosis in the liver and kidneys. T. W. Tunnicliffe, and O. Rosenheim,¹ who made experiments by placing very small quantities of formaldehyde in the food of infants, concluded that formaldehyde added to milk in the proportion of 1 : 5000, or to the entire aliment in the proportion of 1 : 9000, had no appreciable influence on the more important phases of healthy children; but with debilitated children the quantity of urine and dried feces was increased, and the excretion of lecithin decreased. There was no unfavorable influence noted upon the general health of any other children. The proportion of formaldehyde used in milk was considerably in excess of the amount necessary for ordinary preservation.

CARBOFORMAL. The use of carboform in blocks for the purpose of disinfecting rooms, etc., is recommended by both Dr. Dieudonné and Dr. Erne.² Each block contains 50 grammes (12 drachms) of paraformaldehyde, and when lighted glows slowly, but does not burn with a flame, and is said to liberate formaldehyde in the form of gas. When disinfecting rooms by this method it is important that all exposed substances should be thoroughly moistened, which may be accomplished by pouring boiling water over red-hot stones, thereby developing steam. In Dieudonné's experiments, six blocks for each cubic metre were sufficient to kill all forms of bacteria with which it came in contact, and which had been exposed to it for seven hours. It even destroys the activity of the spores of anthrax.

PARAFORM. The statements of A. A. Young³ that when paraform is heated it is vaporized, but upon cooling deposits crystals of para-

¹ Journal of Hygiene, April 27, 1901; Centralblatt f. Physiol., April 27, 1901.

² Münchener med. Wochenschrift, October 16, 1900, and November 27, 1900.

³ Therapeutic Gazette, February 15, 1901.

form, are contrary to the general belief that the vaporization of this substance by heat converts it into formaldehyde.

Guaiacol. Before the therapeutic section at the meeting of the International Congress of Medicine in Paris, Weill and Diamantberger¹ presented a communication in which they claim to have been the first in France to use guaiacol hypodermically in the treatment of pulmonary tuberculosis. They believe that in order to secure the greatest benefit in this disease "intensive and daily guaiacolization," combined with dietetic and hygienic treatment should be continued for a period of not less than seven months, with interruptions of from eight to ten days every three weeks. They attribute the good results shown by the use of the remedy in their hands, to the purity of the guaiacol employed, and the freedom with which it was administered. The following formula was employed by them :

R.—Crystallized guaiacol	3 ijs.	gm.	10.00
Sterilized oil of sweet almonds	3 ijs.	c.c.	10.00
Cocaine hydrochlorate	gr. iij.	gm.	0.20
Sterilized distilled water	3 v.	c.c.	20.00

Place in a dark bottle and keep tightly corked.

Sixteen minims (1.00 gramme) of this solution were administered hypodermically or intramuscularly into the gluteal region once a day.

A space of from 8 to 10 centimetres square on the chest wall is painted with the solution each night, and from forty to fifty drops in three ounces of tepid milk are given by enema at night.

In addition the following pill is given every two, three, or four hours :

R.—Guaiaco (cryst)	gr. j.	gm.	0.06
Terpine (cryst)	gr. jss.	gm.	0.10
Acid. benzoic	gr. ij.	gm.	0.12
Ext. belladonnæ	gr. $\frac{1}{6}$	gm.	0.006
Ext. hyoscyami	gr. $\frac{1}{6}$	gm.	0.006

Misce. To make one pill.

For the last eleven years they have employed this treatment, and have a record of more than 500 cases treated and considerably ameliorated by the systematic use of guaiacol.

Guaiacol appears to be a more valuable topical remedy than an internal one. Its antipyretic effects when applied locally are well known, and a year ago attention was called to the paper of Christian, who made local applications of guaiacol with good results in the treatment of acute epididymitis. In a recent paper, Berthold and Goldberg² report twenty-four cases of gonorrheal epididymitis in which the following ointment was used with good results :

¹ British Medical Journal, October 3, 1900.

² Centralblatt f. innere Medicin, April 6, 1901.

R.—Guaiacol	gr. lxxv.	gm. 5.00
Lanolin	℥ ijss.	gm. 10.00
Resorcin	℥ ijss.	gm. 10.00

Misce ft. unguentum.

Sig.—Apply every twelve hours in such quantities as to use all of it in the course of three or four days.

The patient should be directed to cleanse the parts well and then apply the ointment to the scrotum and cover with a linen rag, absorbent cotton, and wax paper, the whole being held in place by a suspensory. In addition he is directed to take from 3 to 4 grammes (45 to 60 grains) of salol a day. Out of twenty-two patients treated by this method he claims that sixteen were sick less than three days, and some of them did not cease their daily work. Dr. Jesse Hawes¹ presents guaiacol as a remedy of considerable value (applied locally to the urethra) in the treatment of those cases of painful urination where the cause is located in the extreme inner portion of the urethro-vesical orifice. His method of making the application is to pass an ordinary urethral speculum (of as large a calibre as can be borne with comfort) through the deep urethra, and after cleansing away the blood and mucus with absorbent cotton, apply the guaiacol with a small cotton swab to the congested membrane. The mucous membrane should not be covered with the fluid, barely enough to make a surface application is all that is desirable. The application may be repeated at intervals of from five to ten days. It is stated that 25 per cent. of his cases had been cured, 70 per cent. markedly improved, and that in some of the cases where guaiacol had been used there was no benefit derived. Remarkable results are claimed by Allahverdiantz² in the treatment of varices and effusions by painting with guaiacol, and covering with cotton and oil silk. He states that he has cured seven cases of varices of from three to seven years' standing which had been rebellious to all other measures, and also three of varicocele, five of hemorrhoids, and two of hydrocele. He claims that the treatment is also of value in pleurisy with effusions and cedema of all kinds. It will not be amiss to call attention to the fact that local applications of guaiacol not infrequently produce marked lowering of the temperature to below normal, cyanosis, and other symptoms characteristic of poisoning by acetanilid and similar coal-tar derivatives.

Hedonal. During the past year numerous articles have appeared praising hedonal as a hypnotic in cases of insomnia not due to pain. Its dose is from 15 to 30 grains (1.00 to 2.00 grammes) for adults, and is best administered in cachets or dissolved in whiskey, wine, or some

¹ Journal of the American Medical Association, December 29, 1900.

² Bull. Gén. de Thérapeutique, February, 15, 1901.

other alcoholic solvent. Nawrateski and Arndt¹ state that in doses of 45 grains (3.00 grammes), there is no change in the pulse, respiration, or temperature, and that sleep comes on in about thirty minutes, and lasts from two to nine hours without interruption. They have found the drug to be a diuretic of considerable power, and patients to whom it has been administered have a desire to urinate as soon as they awaken, and in some cases this desire interrupts the sleep.

Honthin. This is a tasteless and odorless compound of tannin, albumin, and keratin. It is insoluble in water and only partially soluble in alcohol, and is given in doses of from 5 to 20 grains (0.30 to 1.30 grammes) for adults, and in from 2 to 5 grains (0.12 to 0.30 grammes) for children. It is employed as an intestinal astringent, and is said to pass through the stomach almost unchanged. Joseph Reichelt² and Frieser³ use the drug with good results in the treatment of diarrhoeal diseases of adults and children. The following prescriptions illustrate convenient methods for prescribing :

R.—Honthini 3j. gm. 4.00
Fiant chartule No. xii.
Sig.—One powder every two hours.

For diarrhoea with intestinal fermentation (after cleansing the bowels of their contents by means of an active purge), the following may be administered :

R.—Honthini 3j. gm. 4.00
Mistura cretæ f ʒ ij. c.c. 60.00
Misce. (Shake well.)
Sig.—Teaspoonful every two hours.

Hydrogen Peroxide has been extensively employed as a cleansing agent in the treatment of pus cavities, sinuses, and in fact all discharging wounds which are sufficiently open to permit the free escape of gas which is generated when the peroxide of hydrogen is brought in contact with pus. As its antiseptic and bactericidal power has been questioned, it is interesting to note that both Müller⁴ and Honsell⁵ state that from clinical use and experimental studies, a 3 per cent. solution (by weight) compares favorably as an antiseptic with other substances used for this purpose. C. Moreau⁶ reports a case in which hydrogen peroxide applied to an amputation wound disorganized the occluding clots and caused

¹ Therapeutische Monatshefte, Heft 7, 1900.

² Wiener klin. Wochenschrift, September 6, 1900.

³ Therapist, January 15, 1900.

⁴ Deutsch. med. Wochenschrift, November 15, 1900.

⁵ Beiträge zur klin. Chirurgie, Band xxvii., Heft 1.

⁶ Gazette med. Belge, February 7, 1901.

the catgut ligatures to come untied, entailing secondary hemorrhage, with a fatal result. L. Duncan Bulkley,¹ referring to the use of hydrogen peroxide in dermatology, says that it is being used with increasing confidence in the treatment of chloasma, and for the purpose of bleaching superfluous hair on the face and elsewhere, and that it appears to have a measure of effect in destroying the life of the latter. One of the valuable uses of hydrogen peroxide is its application for the removal of powder stains from the face. J. Neely Rhoads² records its successful use in the treatment of the case of a woman whose face had been burned and blackened by powder. Ten days after the injury the woman applied to him for treatment, and stated that immediately after the accident, and several times thereafter, futile attempts had been made to pick the powder out of her skin. On her first visit to him he tried to extract the grains, but the process was so tedious and painful he began to consider other ways of removing them. At her next visit he applied a solution of hydrogen peroxide, full strength, and gave the patient a bottleful to use at home. Two days later she returned with the powder stains all removed. Dr. Colin R. Clark³ places on record a severe case of burning and staining of the whole face and neck by powder, which was successfully treated by the application of hydrogen peroxide.

Dr. S. E. Wertman⁴ states that not infrequently the skin of coal miners is permanently stained by small pieces of coal becoming embedded, and that he had often successfully employed hydrogen peroxide for removing the stain. Regarding the priority of this method of removing powder stains, Dr. F. K. Smith calls attention to the fact that in the *Cleveland Medical Gazette* of January, 1897, vol. xii., p. 184, will be found a report of the procedure presented by Dr. George W. Crile, of Cleveland.

Ichthyoform is a brownish powder made by a combination of ichthyol and formaldehyde, and is very sparingly soluble in water, and somewhat more so in alcohol. It is said to possess the analgesic astringent and alterative action of ichthyol and the antiseptic properties of formaldehyde. In doses of from 10 to 30 grains (0.6 to 2.00 grammes) daily, it is claimed to have been used successfully as a gastro-intestinal antiseptic. Polacco⁵ praises its therapeutic effect in the treatment of diarrhœa due to intestinal tuberculosis, or typhoid fever.

R.—Ichthyoformi ʒij. gm. 8.00
 Pone in capsulas No. 1.
 Sig.—From two to four capsules every three or four hours.

¹ Journal of the American Medical Association, March 23, 1901.

² American Medicine, April 6, 1901.

³ Ibid., June 1, 1901.

⁴ Ibid., July 6, 1901.

⁵ Treatment, February, 1901.

Iodine and its Compounds. A review of the current medical literature impresses us with the number of well-known and reliable writers who are using iodine compounds in the treatment of tuberculosis. The treatment is by no means of recent origin, nor are any exaggerated claims made as to its curative results, but we believe it is being more generally practised than ever before, that the cases where it is applicable are more fully understood, and that in carefully regulated doses the methods of administration have been improved. The only cases of pulmonary tuberculosis to which the remedy is suited are the incipient ones, before there has been any great destruction of the lung tissues, or before the patient has become exhausted by a long, lasting, mixed infection. In addition to its use in pulmonary consumption, the drug has been valuable in tubercular peritonitis and in glandular tuberculosis. The knowledge that iodine and iodides, when given by the mouth, frequently upset the digestion, and are harmful when given in overdoses to tubercular subjects, and that many persons exhibit marked idiosyncrasies against them, has brought about the use of a number of new compounds. Doses are most carefully regulated, and the hypodermic and inunction method of administration is resorted to in many instances. Spolverini¹ reports remarkable results from the use of intravenous injections of iodine in the treatment of scrofulo-tuberculosis in children, and of syphilis in adults. The formula which he employed is :

R.—Potassium iodide	gr. xiv.	gm. 3.00
Metallic iodine	gr. xv.	gm. 1.00

Sterilized distilled water in sufficient quantity to make 3 ounces or 100 grammes.

He begins with small doses, and gradually increases to the point of tolerance, but in no instance does he think a dose of 5 centigrammes ($\frac{1}{8}$ grain) of iodine administered intravenously at a single injection should be exceeded. The tolerance to the usual dose was generally perfect, except in a few cases where phlebitis was threatened. In one case 28 centigrammes ($4\frac{1}{2}$ grains) of iodine were injected into the vein without any bad effects. In the formula of Spolverini each gramme (16 minims) of the solution represents 1 centigramme ($\frac{1}{8}$ grain) of iodine ; therefore, the maximum dose of 5 centigrammes ($\frac{1}{8}$ grain) of iodine is represented by 5 grammes (80 minims) of the solution. Among the newer iodine compounds which have been brought forward as substitutes for the alkaline iodides (and iodoform under certain conditions) are *iodol*, *europfen* and *iodopin*. Dr. Mellor Tyson² reports the results of his treatment in pulmonary tuberculosis by inunctions of iodol in olive oil. In the incipient cases there was marked improvement in the various symptoms, but no cures. In the advanced cases the improve-

¹ Gaz. degli Ospedali, May 12, 1901.

² Journal of Tuberculosis, January, 1900.

ment was only temporary. In patients doing well under iodol there was an increase in strength and weight, the cough was less frequent and harassing, the expectoration was less profuse, and there was improvement in the digestive symptoms, appetite, and physical signs. The treatment by iodol consisted in daily inunctions of a solution containing 20 grains of iodol to the ounce of olive oil. The quantity of this solution employed gradually increased to half an ounce. In addition to the iodol inunction the patient received $\frac{1}{25}$ of strychnine three times a day, good, nourishing food and out-of-door exercise. Iodol is a pale yellow, inodorous, tasteless powder, insoluble in water, but soluble in three parts alcohol, fifteen parts of ether and fifteen parts of oil. It was introduced in medicine as a substitute for iodoform. Flick,¹ in speaking of the value of the iodine compounds, stated that he preferred inunctions of europen in oil to all other iodine compounds. He had formerly used iodol for this purpose, but found that it broke down very readily and was apt to decompose before it could be used by the patient. Europen is a yellowish, amorphous powder, insoluble in water, but readily soluble in alcohol, ether, and fatty oils. It has been extensively employed as a substitute for iodoform. Dr. Alfred Careno Croftan² records his experience with iodopin injections in twenty-seven carefully selected cases of pulmonary tuberculosis. Of the twenty-seven cases under treatment, nineteen were incipient cases with only circumscribed areas of infection in the apices of one or both lungs; eight were cases in which there were large areas of involvement in one or both lungs; seven were cases of mixed infection, and twenty were cases of simple infection. Although at the time of his report it was impossible to state what the ultimate results would be, so far they had been uniformly good. In some of the cases the appetite improved, the cough and night-sweats were less severe, and the patients gained in weight and improved in spirits. The physical signs were modified and seemed to show that the progress of the disease was held in check and rendered latent. At the beginning of treatment, one drop of iodopin (10 per cent.) was injected into the subcutaneous tissues in the gluteal or interscapular region, and the quantity increased one drop each day (carefully guarding against overdoses) until the proper dose was reached, and when symptoms of improvement became apparent the dose given at that time was continued from thirty to sixty days. In no case did the dose exceed 60 minims a day. Bad effects from this mode of administration were never observed. His reason for selecting iodopin in preference to the other iodine compounds was that greater accuracy of dosage could be

¹ Proceedings of the Philadelphia County Medical Society, 1901.

² Journal of the American Medical Association, November 17, 1901.

obtained with this substance, and he considers this essential in the treatment of tuberculosis. He believes that hypodermic injection of iodopin is the only means by which this accuracy can be secured. Each drop of iodopin represents $\frac{1}{25}$ of a grain (0.0025 gramme) of iodine. Iodopin is a liquid containing iodine dissolved in oil of sesame. There are two strengths upon the market, one containing 10 per cent. and the other 25 per cent. of iodine. It is said to be absorbed from the intestines, and is less likely to disturb digestion than the alkaline iodides. Latterly, in addition to its therapeutic application, it has been employed as a diagnostic remedy in testing the motor activity of the stomach. It has been used for diagnostic purposes by F. Werner,¹ S. Heichelheim,² and O. V. Petersson.³

Dr. William Mackie⁴ claims that calcium iodate acts as a destroyer of bacterial products, and also has an inhibitory action on bacterial growth. He uses the drug extensively and considers it an excellent substitute for iodoform. Its advantages over the latter are freedom from odor, prevention of hypergranulation, and checking of fetor. It may be used in aqueous solutions as a mouth-wash and for the purpose of irrigating the urethra, bladder, vagina, and uterus. In doses from 2 to 4 grains (0.12 to 0.25 grammes) he believes it to be an efficient remedy for checking gastric fermentations.

Jez's Antityphoid Extract. Jez's antityphoid extract is a limpid, reddish, alkaline fluid, made by maceration and expression from the spleen marrow, brain, medulla, spinal cord, and thymus taken from rabbits which have been injected with a highly toxic typhoid culture, and killed two or three days thereafter. This substance was first described by V. Jez⁵ in 1899, who at that time reported eighteen cases of enteric fever treated with the extract. Since his last report, two years ago, he has continued to use the extract with asserted satisfactory results. His method of using the fluid is to administer by the mouth a tablespoonful every two or three hours until the morning temperature is reduced to 38° C., and thereafter a tablespoonful three times a day. He claims that reduction in fever should be noted within twenty-four hours from the beginning of treatment, and within forty-eight hours the fever should change from a continuous to an intermittent type, and become entirely normal by the end of the second week. The nervous symptoms are said to be brought under control promptly, the patient, previously delirious or comatose, usually becomes conscious, quiet, and

¹ Wiener klin. Wochenschrift, February 14, 1901.

² Zeitschrift f. klin. Med., 1900, Band xli., Heft 546.

³ Upsala Laekarefoerenings Foerhandlingar, April, 1901.

⁴ Lancet, December 29, 1900.

⁵ Wiener med. Wochenschrift, February 23, 1899.

free from pain twenty-four hours after the treatment is instituted. In addition to the above indications of improvement, Jez claims that the pulse becomes stronger, and attributes the good results to a diminution or complete neutralization of the effects of the typhoid toxins by the antitoxin extract. The extract is said to be harmless, and may be administered in large doses without giving rise to after-effects.

Liquid Air has been used quite extensively by Dr. A. Campbell¹ as a local anæsthetic in minor operations and in the treatment of neuralgia and herpes zoster; also as a cauterizing agent in lupus, epitheliomata, adenoids, polypi, nævi, and other hypertrophies, and in the treatment of carbuncles. For carbuncles he states that only one application is necessary, and that in twelve hours the pain ceases and does not return, and at the end of a few days only a small ulcer is left. The mode of applying the spray for carbuncles is to project it into the opening and use the air quite freely; then thoroughly freeze the external surface, which must be well cleansed of any discharge that may have resulted from sending the air inside the carbuncle. After applying the treatment, a dry absorbent dressing should be put on so that the discharge, which will be abundant, and is accompanied by considerable bleeding, can be readily taken up. He says that the reaction from the freezing takes place after about twenty minutes, and it is to this extreme hyperæmia he attributes the success of the treatment.

Male Fern. Numerous cases of poisoning, and some deaths, have been reported from the use of excessive doses of oleoresin of aspidium, and it is generally thought that 2 drachms (8.00) should not be exceeded in a dose. Dr. Arshag D. Margossian reports five cases in which he employed successfully 4 drachms of the oleoresin at a dose. We can hardly agree with him in thinking such doses safe. F. Dammer² and W. Gotthilf³ each report a case of poisoning following the administration of the drug in much smaller doses. In Gotthilf's case $2\frac{1}{2}$ drachms (10.00 grammes) had been taken, but had not been followed by a purge.

Mercury. The hypodermic injections of mercury in the treatment of syphilis are probably less frequently employed than formerly, because the pain and ulcerations often seen after such injections counteract the slight advantages over the method of administration by the mouth. Dr. Brocq, of Paris, has recently stated that only about one-tenth of his syphilitic patients were treated by inunctions and injections, and he considers it expedient as a general practice to administer mercury by the mouth.

¹ Journal of the American Medical Association, February 16, 1901.

² Münchener med. Wochenschrift, 1900, No. 13, and W. Gotthilf, *Ibid.*, July 2, 1901.

³ *Ibid.*

Dr. Dieupart (in his recently published book on the treatment of syphilis by injections) analyzes the results of 1062 observations in which this method was employed: 78 injections of calomel were followed by rather indifferent therapeutic results, and gave rise to pain and inflammatory nodules, but neither stomatitis nor diarrhœa was present. There were 150 injections of salicylate of mercury, and, although no serious accidents occurred, the curative action hardly seems sufficient. There were 319 injections of gray oil, and, while it appeared to cure slight cases, the injections were frequently followed by stomatitis. There were 15 cases in which solutions of red mercuric iodide in oil were used, and apparently the results were very good, except in cases of visceral syphilis. He regards the best of all formulæ for hypodermic injections of mercury to be the bichloride serum of Cheron. Bailey¹ reports good results in 70 cases of syphilis treated by mercurialized serum, which he considers superior to other mercury injections, being simpler and easier of administration and much less painful. Slight stomatitis was noticed in four of his patients, while clinical recovery followed an average of from three to four injections. The formula of this preparation is as follows:

R. —Corrosive mercuric chloride	gr. lxxv.	gm.	5.00
Sodium chloride	gr. xxx.	gm.	2.00
Boiling distilled water	℥i.	gm.	200.00
Dissolve, and when cold add				
Carbolic acid	gr. xxx.	gm.	2.00

The amount injected averages 20 c.c. during the week.

MERCUROL, or MERCURY-NUCLEID, is a brownish-white powder, soluble in water but not in alcohol. It is non-corrosive and non-irritative, does not precipitate albumin, and has been used internally and hypodermically in the treatment of syphilis, and locally as an antiseptic and germicide. It is said to contain about 10 per cent. of mercury, and, as aqueous solutions are not permanent for more than a week, solutions should be made fresh when desired. Its dose is from $\frac{1}{4}$ to 2 grains, although in cases of syphilis as much as 7 grains three times a day have been well borne. Urethral injections of aqueous solutions in the strength of 2.5 per cent. may be employed in the treatment of gonorrhœa at the beginning, and the strength increased when desired.

MERCURY ETHYLENEDIAMINE. This is a liquid preparation made by dissolving 10 grammes of citrate of mercury and 4 grammes of ethylenediamine in 86 grammes of water. In the strength of 1 to 30, or 1 to 200 in water, it is recommended as a powerful disinfectant for the hands.

¹ Gazette hebdom. de Médecine et de Chirurgie, February 17, 1901.

Methyl Alcohol. Methyl alcohol is a highly toxic substance, and during the past year there have been frequent reports of poisoning from it, some of which have resulted fatally.

The most prominent symptom of poisoning, in addition to the ordinary symptoms of intoxication, is blindness, which comes on suddenly, usually after a debauch, during which the individual has drunk highly purified wood alcohol, or in other cases appears after the individual has partaken freely of tincture of ginger, essence of peppermint, or other liquids in which methyl alcohol instead of ethyl alcohol has been employed as a menstruum or solvent. In other instances mechanics have been poisoned by inhaling the fumes.

Dr. I. Dunn¹ reported two cases in which the blindness followed a debauch, during which time, in addition to other intoxicants, the subject drank freely of essence of Jamaica ginger. These cases, which were not seen by him when the sight was first impaired, improved for a time under treatment, but later there were evidences of atrophy of the optic nerve and further impairment of vision.

Dr. Herbert Harlan² reported two cases of blindness which were attributed to the use of essence of Jamaica ginger and essence of peppermint in which the solvent used was methyl alcohol. Neither case was seen until several months after the onset of the symptoms, and both showed atrophy of the optic nerve. One of these became totally blind and the other almost so.

Dr. E. Stieren³ reports a case of a man whom he saw a few hours after the onset of blindness following the immoderate use of essence of Jamaica ginger containing methyl alcohol. The treatment pursued in this case was as follows: the patient was confined to bed in a dark room; he was given active cathartics, and $\frac{1}{2}$ grain of pilocarpine twice during the night. By the following morning the patient was able to count the number of fingers put before him at a distance of ten inches. Pilocarpine, in the dose of $\frac{1}{2}$ grain given hypodermically, was given at intervals of six hours, and 1-grain doses of calomel given every two hours for the following two days.

After that time the patient was placed upon potassium iodide. His condition gradually improved, so that on the fifth day after beginning treatment his vision in each eye was 20/30, and when last seen, five months afterward, his vision had improved 20/20.

Methylene Blue. In view of the fact that many clinicians have testified to the value of methylene blue in the treatment of malaria, we

¹ Virginia Medical Semi-Monthly, January 25, 1900.

² Ophthalmic Record, February, 1901.

³ Journal of the American Medical Association, January 5, 1901.

are somewhat surprised to find that H. Ziemann¹ considers it practically useless. R. Koch² regards methylene blue as next to quinine in value as a prophylactic and in the treatment of malaria, and particularly valuable as a prophylactic where the hemorrhagic form is suspected. In his studies of the action of quinine and methylene blue, A. Ivanoff³ found that methylene blue affected the protoplasm chiefly and quinine the chromatin. The young forms of the parasite contain very little protoplasm, and consequently are not affected by methylene blue, but succumb rapidly to quinine. The reverse is the case with the adult parasites, which are almost all protoplasm and very sensitive to the action of methylene blue. He furthermore asserts that the crescentic form of malarial parasites is completely resistant to quinine, but is destroyed by the action of methylene blue.

Charles H. Lewis⁴ adds three cases to the twenty heretofore reported in which methylene blue injections were used in the treatment of pleurisy with effusion. This method consisted in withdrawing (under careful antiseptic precautions) a part of the effusion, mixing it with from 5 to 15 grains of methylene blue, and then returning it to the pleural cavity. He states that in the twenty-three cases treated by him the average time required for the reabsorption of the fluid from the pleural cavity was about fourteen days.

Naftalan. This is a peculiar gelatinous substance, made by mixing a purified naphthala obtained from Russia with about 2.5 to 4 per cent. anhydrous soap. It should not be confused with naphthalin. It is devoid of irritative properties, and is said to have been employed with success in the treatment of burns, ulcers, eczema, and pruritus. M. Rauch⁵ has used suppositories containing 20 per cent. of naftalan mixed with cacao butter and a sufficient quantity of white wax to give consistency, in the treatment of hemorrhoids. He states that the pain subsided at once, and that hemorrhage was averted and the nodes partially or entirely disappeared. Voges,⁶ who is at the head of the National Department of Hygiene of the Argentine Republic, states that it acts as a specific in the poison of the bite of the mosquito. H. Sagebiel⁷ testifies to its value in the treatment of eczema.

Orthoform. In the treatment of tubercular ulceration of the larynx, after thoroughly cleansing the part and applying (by insufflation in the larynx) a powder consisting of saccharated suprarenal gland, W. Freu-

¹ Deutsch. med. Wochenschrift, November 22, 1900.

² Ibid., December 13, 1900.

³ Ibid., December 21, 1900.

⁴ Medical News. June 1, 1901.

⁵ Deutsch. med. Wochenschrift, September 27, 1900.

⁶ Anales del Cir. med. Arg. (Buenos Ayres), December, 1900.

⁷ Münchener med. Wochenschrift, November 27, 1900.

denthall¹ applies locally the following emulsion, which relieves the pain, soothes the cough, and permits the patient to take food, and also promotes the healing of the ulcers :

R.—Menthol	gr. xv.	gm.	1.00
Vitelli ovarum	3 vj.	gm.	25.00
Olei amygdalæ express.	3j.	gm.	30.00
Orthoformi	3 iij.	gm.	12.51
Aquæ dest.	3 iij.	gm.	100.00

Misce et fiat emulsion.

As soon as the toleration of the patient permits the menthol is increased up to 10 grammes.

Sprague² found the following prescription valuable in the treatment of hemorrhoids :

R.—Orthoformi	gr. xxxvij.	gm.	2.50
Ung. chrysarobini	gr. xxx.	gm.	2.00
Ung. belladonnæ	gr. xxx.	gm.	2.00
Iodoformi	gr. xxx.	gm.	2.00
Adipis lanæ hydrosi	3 vj.	gm.	25.00

Misce et ft. unguentum.

In burns of the first degree he believes the best remedy to be an ointment composed of 10 per cent. of orthoform, 5 per cent. of ichthyol, and 85 per cent. of lanolin :

R.—Orthoformi	gr. xxxvij.	gm.	2.50
Ichthyoli	gr. xix.	gm.	1.25
Adipis lanæ hydrosi	3 vj.	gm.	25.00

In burns of the second and third degree he finds that a powder composed of equal parts of orthoform and boric acid quickly relieves the pain and promotes rapid healing. For the dermatitis of rhus poisoning he found a combination of orthoform, dermatol, and starch satisfactory. On account of its non-solubility, orthoform is absorbed very slowly, and therefore poisoning from it is less frequent than with the soluble local anæsthetics. When applied in the form of ointments or emulsions it sometimes excites hyperæmia, pruritus, and swelling of the parts to which it is applied. W. Dubreuilh³ states that orthoform is capable of producing two distinct varieties of eruptions—erythema, which may be simple or complicated with vesicles or pustules ; and gangrenous eruptions, which, however, are rare. The gangrenous eruptions are more likely to occur when varicose veins are treated with orthoform. G. Spiess⁴ has employed orthoform insufflations into the larynx in the treatment of whooping-cough. He states that relief is immediate, and

¹ Journal of the American Medical Association, March 16, 1901.

² American Therapist, September, 1900.

³ La Presse Médicale, May 18, 1901.

⁴ Münchener med. Wochenschrift, April 9, 1901.

that infants and children make no resistance to the measure as they learn that it is painless.

Ovarian Extract. The use of ovarian extract in the treatment of disorders associated with menstrual functions appears to be unsatisfactory. E. E. Montgomery¹ states that he has never seen the slightest influence from the use of it. Wilmer Krusen² used ovarian extract in 5-grain doses daily, and, while he was unable to secure any satisfactory or permanent results in the treatment of amenorrhœa and dysmenorrhœa, the drug appeared to modify some of the nervous symptoms which were seen during the artificial menopause. He believes that the use of the extract is based on a false theory, since the ovary has no internal secretion. Walter E. Dixon³ believes that the ovary is a secreting organ, and claims to have seen beneficial results, following the administration of the extract, in women upon whom double ovariectomy had been performed.

Pancreon. Pancreon is a grayish, inodorous powder, made by the action of tannic acid upon pancreatin. It is said to possess strong tryptic, amylolytic, and emulsifying power, and to resist the destructive action of the gastric juice for five hours.

The doses usually employed are 5 to 10 grains (0.3 to 0.6 gramme) during or after each meal. It is said to act best in the presence of mild alkalies.

R.—Pancreon	3j.	gm.	4.00
Cretæ præparatæ	3 ss.	gm.	2.00
Misce et ft. chartulæ No. xii.			
Sig.—One to two powders after meals.			

Peruol. This substance is a benzyl-ester of benzoic acid, and represents the most active element in balsam Peru. It is a clear, odorless oil, which does not irritate the skin or soil the clothing, and, in the proportion of 1 to 3 in castor oil, is fatal to the itch mite. Richard Sachs⁴ treated thirty-five cases of scabies by the local application of peruol and oil, and all improved quickly. In only four was a recurrence noted. The prescription which he found valuable was as follows:

R.—Peruoli	3j.	gm.	4.00
Olei ricini	3 iij.	gm.	12.00
Misce. Sig.—Shake well, and rub thoroughly into the body twice a day.			

He directs that a bath be taken prior to the inunction unless there is too much inflammation of the skin. The usual methods regarding the disinfection of clothing and bedding should be strictly adhered to.

¹ International Medical Magazine, November, 1900.

² American Gynecological and Obstetrical Journal, March, 1900.

³ Practitioner, May, 1901.

⁴ Deutsch. med. Wochenschrift, September 27, 1900.

Pilocarpine Hydrochlorate. We have no recollection of having had our attention called heretofore to the value of pilocarpine in the treatment of membranous croup, but the report of Dr. S. E. Wertman¹ indicates that it is a valuable remedy. He gives histories of five severe cases of croup in children (bacteriological examination not made), ranging in ages from thirteen months to ten years, in which he attributes the recoveries to the hypodermic injections of $\frac{1}{8}$ grain of the hydrochlorate of pilocarpine. In only one of these cases was the injection repeated, and in three of the five cases false membranes were visible upon the pharynx and tonsil.

Pituitary Extract. The pituitary body is known to consist of two parts, the posterior lobe or infundibulum, which furnishes an extract which, when injected into the veins, will raise the blood-pressure and increase the heart's action; and the anterior part, or hypophysis, which does not furnish any such secretion. While there have been numerous reports testifying to the value of the pituitary extract in relieving certain of the symptoms of acromegalia, there are also reports which state that the extract has been found to be without value. Is it not possible that different parts of the gland were employed by the different observers?

O. S. Osborne² reports three cases of acromegalia in which he tried pituitary feeding. The first case was in the last stages of the disease and died three or four months after the treatment was begun. In the second case the persisting headache and a considerable amount of the hypertrophy of the lips, hands, and feet disappeared under pituitary treatment, and the patient gained greatly in muscular power. In this case, if the pituitary extract were stopped, the symptoms redeveloped, but were again arrested as soon as the treatment was reinstituted. In the third case the patient developed an intense and persistent earache, for which no cause could be found, and, being placed upon pituitary treatment, the pain entirely disappeared. At the fifty-second meeting of the American Medical Association, Dr. Sydney Kuhn³ stated that in two out of three cases of acromegalia treated with powdered extract of pituitary body the subjective symptoms were relieved and nutrition improved. If the medicine was discontinued there was redevelopment of the symptoms.

Pyramidon Bicomphorate. This is a yellowish-white, crystalline powder with a camphoraceous odor, which, in doses of from 1 to 5 grains (0.06 to 0.3 gramme) has been used as an antipyretic and analgesic. Its advantage over pyramidon is that it does not produce the

¹ American Medicine, July 6, 1901.

² Journal of the American Medical Association, March 23, 1901.

³ Philadelphia Medical Journal, June 23, 1901.

profuse perspiration seen after the administration of the last-named substance. Bertherand¹ employed the drug, hypodermically and by the mouth, in the treatment of sciatica, for reducing the fever in pulmonary tuberculosis and for relieving the pain in rheumatism. In discussing this drug it will not be amiss to call attention to the observations of A. Robin and G. Bardet,² that in diabetes it markedly increases the amount of sugar in the urine. A convenient method of administering pyramidon bicamphorate is as follows :

R.—Pyramidon bicamphoratis 3ss. gm. 2.0

Pone in capsules No. xii.

S.—One to two capsules not oftener than every four or six hours.

Quinine. Methylene blue, guaiacol, and a number of other drugs are reputed to be of decided value in the treatment of malaria, but none is as sure to break up an attack as quinine, and, unless there exists some contraindication to its use, it should be invariably employed in severe cases. Manson³ is so thoroughly convinced of its power that he says "it may safely be asserted that any intermittent fever which resists quinine for three or four days is not malarial." There are several questions, however, relating to the use of the drug in malaria upon which authorities differ. In the first place, there is considerable diversity of opinion as to whether, in the presence of an ordinary intermittent malaria, the full dose should be given during the sweating stage, so as to affect the young parasite, or whether it should be administered an hour or two before the expected paroxysm, so as to act upon the fully developed organism. It is customary in this country to give full doses an hour or two before the paroxysm, in order to have the patient cinchonized at that time. Until the question is fully settled on a scientific basis it seems safe to follow this plan, for, though the chill should not be aborted, the drug will be in the blood at the time of sporulation. Another question upon which authorities and men of practical experience differ widely is the advisability of using quinine in the treatment of malarial hæmoglobinuria. From a review of the current literature it is impossible to come to any conclusion relating to the curative action of quinine in the disease. As the parasitology of hæmoglobinuria is far from being settled, we cannot take the middle ground and advise its administration in some cases and not in others. If the disease is due to a parasite destroyed by quinine the drug should be given; if not due to such a parasite it is harmful. We see no hope of this question being settled as long as quinine is empirically used in these cases. The subject is being diligently studied, and there is every

¹ Bulletin Thérap., February 23, 1901, and Semaine Médicale, May 1, 1901.

² Les Nouveaux Remèdes, 1900, No. 15.

³ London Practitioner, March, 1901.

reason to believe that in a few years the parasitology will be known, and soon thereafter the effect of quinine on the disease determined.

Dr. M. H. Fussell¹ speaks enthusiastically of the beneficial effects of quinine in properly selected cases of slow labor due to uterine inertia. He deplores the fact that a drug so valuable in certain of these cases is being employed to such a limited extent. He has used quinine for a number of years and in many cases of labor, and finds it of most value in multiparæ in whom the os is much dilated and with slow and ineffectual pains. In such cases 15 grains of quinine will frequently obviate the necessity for using forceps. When labor is delayed by reason of some disproportion between the size of the head of the child and the pelvis of the mother, or when, from malposition, the head fails to engage, quinine should not be given. In addition to its value as a stimulant during the second stage of labor, he finds that the loss of blood after labor is considerably diminished. Dr. Jaboulay recently called attention to the improvement in all the symptoms of carcinoma following the hypodermic injections of soluble salt of quinine into and about the neoplasm. Later he discovered it to be quite as effective when given by the mouth. He gives 1 gramme of quinine a day, substituting Fowler's solution two days each week. In addition to this he applies to the growth 10 per cent. quinine ointment. Launois, before the Société de Chirurgie, February 20, 1901, reported a case of inoperable carcinoma of the breast in which some of the symptoms had been improved by the hypodermic use of soluble salt of quinine.

Silver Nitrate. At the fifty-first annual meeting of the American Medical Association, Dr. Thomas J. Mays² stated his reasons for using silver nitrate injections in the treatment of pulmonary consumption, and reported a number of cases, with histories, in which this treatment had been employed. As is well known, it is his belief "that the nervous system is generally, and the pneumogastric nerves are especially, implicated in pulmonary consumption, and that any therapeutic agent which affects this disease favorably and permanently either appeals directly or indirectly to the pulmonary organs through the nervous system." He also believes any influence or agent having the power to undermine the integrity of the nervous system also has the power to generate pulmonary consumption or some form of pulmonary disease. Some years ago he employed for a time massage, kneading, and compression of the pneumogastrics through the overlying tissues of the neck, and while he claimed to have observed that the cough, expectorations, and general condition of the patient were improved, the stimulus he was thus

¹ Therapeutic Gazette, January 15, 1901.

² Journal of the American Medical Association, January 19, 1901.

able to apply to the nerves was not sufficiently powerful to make it of decided value. He thinks if some conservative irritant, like nitrate of silver, could be injected immediately over the course of the nerves in the neck it might furnish the stimulus necessary to modify the morbid condition of the lung. After many trials he found the best results could be obtained by the subcutaneous injections of 5 minims of a 2.5 per cent. solution of silver nitrate, which should be preceded by 5 minims of a 2.5 per cent. solution of cocaine. His method of procedure is about as follows: the skin immediately over or slightly behind the pulsating carotid artery in the neck (between the angle of the lower jaw and the clavicle) is lifted between the thumb and forefinger of the left hand and the needle just pushed through it. The cocaine solution is now injected, and, without withdrawing the needle, the syringe is detached, washed, and then the nitrate of silver solution injected. Considerable pain, and sometimes diffuse swelling, for some days follows this injection, and, except in cases of severe cough, they are not repeated for a week or ten days. The injections, as a rule, are administered in the region of the pneumogastric nerves supplying the affected lung.

UNGUENTUM CREDÉ (Crédé's ointment of soluble metallic silver). That inunctions of this ointment (of which the formula is given on page 403 of *PROGRESSIVE MEDICINE*, December, 1900) are capable of favorably influencing septic infections we have been able to verify on several occasions. Crédé¹ states that the best method of employing it is to first wash the skin, and by friction produce hyperæmia; then rub in 2 or 3 grammes of the ointment. By this means he has been able to arrest threatened suppurations of inflamed glands, and he believes, if the treatment is begun early enough, phlegmons can be aborted. He has also used the ointment with gratifying results in feverish conditions (observed about the third day) in lying-in women, in erysipelas, cerebrospinal meningitis, acute rheumatism, typhoid fever, and pneumonia. N. S. Davis, Jr.,² reports a case of malignant endocarditis in which recovery followed daily inunctions with the ointment. P. Viêt³ considers it a specific in sepsis, and especially valuable in country practice. He employed the ointment in larger doses than usual; for adults, as much as 12 grammes (3 drachms) in nine hours; for a child of seven years of age, 8 grammes (2 drachms) in eight hours; and 2 grammes (30 grains) a day for an infant of two months.

F. Daxenberger⁴ has used from 2 to 3 grammes (30 to 45 grains) of Crédé's ointment, with good results, in the treatment of acute menin-

¹ Medical Press and Circular, December 26, 1900.

² Journal of the American Medical Association, January 5, 1901.

³ Allg. med. Central. Zeitung (Vienna), January 23, 1901.

⁴ Klin. Therap. Wochenschrift, May 12, 1901.

gitis. In such cases he believes the ointment should be well rubbed into the skin of the head and neck, and that at least fifteen minutes should be spent in making the inunction.

COLLARGOL. The statements of Gindes and Balardzsheff,¹ who made both laboratory and clinical studies of the germicidal action of collargol, distinctly contradict the assertions of Schlossmann, who claimed that it was far superior to bichloride of mercury as a germicide. They found that aqueous solutions of collargol in the strength of 1 to 1000, 1 to 500, and 1 to 100 for twenty-four hours, and 5 to 100 and 15 to 100 for one hour failed to kill anthrax, staphylococcus, or streptococcus.

Credé's ointment was used by them in treating scarlet fever and other infectious diseases, and they failed to observe any beneficial effects from its use.

Sodium Cacodylate. The ordinary salts and preparations of arsenic are of very great therapeutic utility, but their field of usefulness is limited to a certain extent by reason of the fact that when administered in full doses over a prolonged period they irritate both the gastro-intestinal tract and other tissues. It is claimed that the organic compounds of arsenic known as the "cacodylates" are almost entirely free from such deleterious effects, and that they may be given in full doses and for long periods (with occasional interruptions) without any harmful results. It was at first thought they were entirely free from any of the toxic effects of arsenic, but experience has shown this to be incorrect.

The most popular of the organic arsenate compounds is sodium cacodylate or sodium dimethyl arsenate. It is a white, amorphous powder, soluble in water, tasteless, and inodorous. It is very rich in arsenic, $1\frac{1}{2}$ grains (0.10 gramme) are equivalent to about 1 grain (0.06 gramme) of arsenous acid, or 3 grains (0.18 gramme) of sodium arsenate. Being an expensive product (five or six dollars an ounce), the temptation to adulterate or substitute is greater than with cheaper drugs. It is of the utmost importance in prescribing this salt to see that the chemically pure article is furnished, as the commercial article is often contaminated by cacodyl oxide and other impurities, which cause a garlicky odor of the breath and other disagreeable effects. The dose of this salt at the beginning of treatment is from $\frac{1}{4}$ to 1 grain (0.01 to 0.06 gramme) daily, but this dose is sometimes increased to 10 grains (0.65 gramme) or more a day, and continued for several weeks without harmful effects. Gauthier believes the drug should never be administered in any other way than hypodermically, but others assert

¹ Russki Archiv Patologii, Klinitcheskoi Mediciny i Bakteriologii, June, 1901.

that it acts quite as well if given per os or per rectum. The salt is said to markedly increase not only the leucocytes, but also the erythrocytes. It increases the processes of oxidation and confers upon the economy the power of strongly resisting morbid influences. Gauthier and others who have employed it extensively assert that they have seen remarkable results follow its application in the treatment of tuberculosis, asthma, chorea, diabetes, neurasthenia, profound anæmia, malarial intoxication, myxœdema, vomiting, dry, scaly skin diseases, and in anorexia and debility following exhausting diseases. In fact, it is applicable to all of the diseased conditions in which arsenic has heretofore been of value. The formulæ of Gauthier for hypodermic injections will be found on page 332 of *PROGRESSIVE MEDICINE*, December, 1900. The following prescription will be found suitable for administering this drug in pill form :

R.—Sodii cacodylatis	gr. iv.	gm. 0.25
Cerati resinæ	gr. i.	gm. 3.30
Misce et fiant pilulæ No. xxiv.		
Sig.—One to three pills three times a day.		

Suprarenal Extract and Adrenalin. Judging from the literature of the past twelve months, the value of suprarenal extract has been fully sustained in the treatment of Addison's disease, hay fever, as an astringent to the mucous membranes, as a powerful and rapidly acting vasomotor stimulant, and as a hæmostatic. Several writers report new applications of this substance, where it has been successfully employed, Dr. William H. Bates¹ considers the suprarenal gland the most powerful of hæmostatics and astringents, and the only one which can be instilled into the eye and applied to the most delicate mucous membrane without giving rise to injurious effects, unless, of course, continued for a long period. The constringing effect of this or any powerful astringent will interfere with the nutrition of the part upon which it is applied if it is constant. In deafness resulting from the inflammation of the Eustachian tube he found local applications of the solution of this substance improved the hearing where all other treatments had failed. In his hands most satisfactory results have been obtained from a freshly prepared mixture of 1 part of the dry and powdered gland with 4 parts of water, which when used in the eye or ear should be filtered. Sterilization by heat does not alter the efficacy of such a solution. In some cases he believes that the internal application of the gland will control hemorrhage. Gleason² praises the hæmostatic and astringent effect obtained by the local use of the gland in diseases of and operations on the nose,

¹ New York Medical Record, February 9, 1901; International Medical Magazine, December, 1900.

² International Medical Magazine, November, 1901.

ear, and larynx. He considers it a mistake, however, to suppose it is possible by its use to control hemorrhages from large arteries. In cases of earache, where the intratympanic mucous membrane is exposed from previous perforations of the drum-head, an attack of acute otitis media can usually be aborted by the instillation of a few drops of sterile 10 per cent. solution of the suprarenal gland. The liquid should be removed after a few minutes by means of absorbent cotton, in order to prevent putrefaction. He speaks enthusiastically of the combined external and internal applications in hay fever. Dr. Daniel McKenzie¹ cites a case of active hemorrhage in a hæmophilic boy, aged thirteen years, where the local application of tannin, plugging of the nostrils, and an internal application of calcium chloride failed to permanently control the bleeding. The local application of a watery solution of the suprarenal gland immediately stopped the hemorrhage. Several hours later there was a slight recurrence of the bleeding, which was effectually and permanently controlled by a second application of that agent.

Dr. Lewis S. Somers² reports two extreme and obstinate cases of nasal hemorrhage where the usual procedures had failed to control the bleeding, which were then successfully treated with a sterilized solution of suprarenal extract. He does not believe the value of the extract in such cases is limited to the temporary vascular constriction produced by it, but that erosions are healed and a general nutritive tone given to the tissues that no other local remedy seems to possess. In the treatment of fourteen cases of hæmoptysis, W. B. Kenworthy³ reports very satisfactory results from the use of 3-grain powders of dried suprarenal extract every half-hour until three doses were taken, then every two hours until three more were taken, and then one three times a day for a week. He claims that the best effects will be obtained if the drug be taken dry on the tongue and swallowed without water. In the fourteen cases of pulmonary hemorrhage thus treated, in only one did the hemorrhage continue beyond fifteen minutes after the first powder had been taken. S. Floersheim⁴ also employed the drug in the treatment of hæmoptysis, and, while his results were favorable, he does not consider the beneficial effects from the use of the drug as definitely settled.

The benefit resulting from its use in cases of rhinitis, acute tracheo-bronchitis, chronic bronchitis, congestion, and œdema of the lungs he believes to be more positive. Acute bronchitis when treated from the onset was generally cured in twenty-four hours. He thinks that the good results obtained from the use of the extract in cases of congestion

¹ British Medical Journal, April 21, 1901.

² Philadelphia Medical Journal, March 2, 1901.

³ Medical Record, March 16, 1901.

⁴ Ibid., November 17, 1900.

and oedema of the lungs are not limited to the constricting effects on the bloodvessels, but that it also has a stimulating effect on the heart.

In hematemesis, O. F. F. Grunbaum¹ considers small and frequently repeated doses of suprarenal extract to be of positive value. In hemorrhage from the bladder and post-partum hemorrhage he believes the best results can be obtained by irrigations with a sterilized solution of the gland. On account of its powerful action in stimulating muscular contraction, and particularly as he found it to be a powerful stimulant to uterine contractions, either when given by the mouth or applied locally, E. A. Schaffer² strongly recommends it in cases of post-partum hemorrhage. In such cases he believes the best results are to be secured by injections, directly into the uterus, of a sterilized aqueous solution containing 30 grains of the dried medullary substance of the suprarenal gland and 60 grains of calcium chloride in a pint of water. Dr. O. T. Osborne³ considers a strong solution of the gland valuable as a local application for all cases of capillary hemorrhage where the bleeding surface can be reached, such as the stomach, rectum, large intestine, bladder, vagina, uterus, and also in cancerous conditions. When solutions are applied to the uterus or bladder they should be followed by irrigation with a mild antiseptic solution, on account of the tendency to decomposition.

In Addison's disease, suprarenal extract has been used with curative effects in some cases and with great benefit in many others, and is without doubt the most valuable agent we possess in the treatment of this disease; but there are cases in which the drug is without any appreciable effects. Dr. O. T. Osborne⁴ gives as a possible reason for its failure in some cases the fact that the disease may be due to some other functional or pathological condition, and that a pathological condition of the suprarenal gland may be only one of the causes of the disease. It is well known that we have Addison's disease with degeneration of the suprarenal and intact suprarenal gland, and an extensive degeneration of these glands may exist without Addison's disease being present. Dr. Charles R. Box⁵ reports six cases of Addison's disease under careful daily observation in which the gland was used. He concludes from the study of these cases that either the active substance had not been properly administered, or that the requisite material is not contained in the suprarenal bodies as at present prepared for administration, or that the lack of a certain internal secretion is not the sole or predominant factor in Addison's disease. The report of numerous cases by P. Edel⁶ and

¹ British Medical Journal, November 3, 1900.

² Ibid., April 27, 1901.

³ Journal of the American Medical Association, March 23, 1901.

⁴ Ibid., March 23, 1901.

⁵ Practitioner, May, 1901.

⁶ Münchener med. Wochenschrift, December 25, 1900.

Anderodias¹ and other writers during the past year confirm the previous reports of the great value of this agent.

Its value as a cardiac stimulant has not yet been definitely settled. Osborne² says that we cannot raise the vascular tone nor combat cardiac weakness with suprarenal gland given hypodermically or by the stomach, while W. H. Bates³ claims that it is the most powerful heart tonic known, and that within three minutes after the injection of 5 grains of the dried gland the weak pulse of organic heart disease becomes stronger and the high tension pulse of the laboring heart becomes regular; also, that the normal heart is not embarrassed by the administration of as much as an ounce of the powder. S. Floersheim,⁴ in an attempt to determine clinically the effects of suprarenal extract, experimented with several normal cardiac cases and some which were not normal. He found when the heart was weak and irregular that usually within a short period—in some cases as early as ten seconds and in others as long as ten minutes—after the powdered extract had been chewed and swallowed the pulse became fuller and the heart much stronger and more regular in its action. The effects of the drug are quickly manifested when thus taken, but pass away with equal rapidity and without permanent results. Upon the normal heart, he claims, there is no influence from the use of the drug, and in cases of organic heart disease the pulse is not affected when it is normal.

E. A. Schaffer⁵ believes, from the results of his experiments upon animals, that the intravenous injection of 5 grains to the ounce of a sterilized solution of the extract of the gland should be of the greatest value in cases of sudden cardiac failure, for the relief of shock and overdose of an anæsthetic. The solution should be administered slowly into the vein with a hypodermic syringe, or, in extreme and hopeless cases, directly through the thoracic wall into the heart muscle.

One of the principal disadvantages of the suprarenal extract is that aqueous solutions rapidly deteriorate. Among the different antiseptics and preservatives recommended to be added in small quantities to these solutions are boric acid, carbolic acid, resorcin, and chloreto-ne. We do not believe that any of these substances are satisfactory, but chloreto-ne, in addition to its antiseptic properties, is a local anæsthetic, and is the most practical when the solution is intended to be used locally.

ADRENALIN. In the *Therapeutic Gazette* of April 15, 1901, Dr. Jokichi Takamine makes a preliminary report of his discovery and

¹ Journal de Médecine de Bordeaux, 1900, No. 29.

² Journal of the American Medical Association, March 23, 1901.

³ International Medical Magazine, December, 1900.

⁴ New York Medical Journal, October 6, 1900, and May 18, 1901.

⁵ British Medical Journal, April 27, 1901.

isolation of the blood-pressure raising principle of the suprarenal gland. This active principle, which he designates as adrenalin, is described by him as a light, white, micro-crystalline substance, showing itself thus far in five different forms of crystals, which vary according to the conditions of the solutions from which they are made. Furthermore, the crystals can be transformed by different methods of recrystallization. The different shapes the crystals may assume are "wart or tomato shape, boat or leaf shape," rhombic plates and their agglomeration, fine needles and prism shapes. It is slightly bitter to the taste, and benumbs the tongue when placed upon it. It is sparingly soluble in cold water, but more so in hot. From a hot saturated aqueous solution the crystals separate upon cooling. The substance is perfectly stable when dry, but is easily oxidized, and changes its color when aqueous solutions are exposed to the air. Adrenalin is easily soluble in alkalies, but not in ammonium hydrate or solutions of alkaline carbonates. By experiments he has shown it to be a very powerful astringent upon mucous membranes and a vasomotor and heart stimulant. A fraction of a drop of a 1 to 10,000 aqueous solution blanches the normal conjunctiva in from thirty to sixty seconds. The intravenous injection of 0.000016 gramme of adrenalin chloride powerfully raises the blood-pressure in dogs. Comparing its strength as a vasomotor stimulant with that of fresh extract of suprarenal gland, he found adrenalin to be 625 times more powerful, and, making allowances for mineral impurities in the adrenalin, he believes it to be 1000 times stronger than an extract of a fresh gland. Clinically, the substance has been found to be applicable to all those diseased conditions in which the suprarenal extract has heretofore been found valuable. We believe the isolation of this principle to be one of the most important epochs in materia medica during the past year. We find it difficult to believe that a drug so powerful as adrenalin is, as stated by Takamine, non-poisonous and possessed of no injurious properties. In thirty-five cases of rhinological operations adrenalin was employed as an astringent and hæmostatic by Dr. Emil Mayer,¹ who was much pleased with it. He found there were no constitutional effects from the use of the drug, and believes it may be safely applied to persons of all ages of either sex; also, that a 1 to 1000 solution is very strong and sufficient for operative cases, and 1 to 5000 or 10,000 for every purpose of local medication. He considers the tablets the most convenient method of making the solution, which, after being kept for a time, slowly changes color, becoming pink, brown, and finally muddy and flocculent; but these changes in its physical appearance have no effect upon the remedy.

¹ Philadelphia Medical Journal, April 27, 1901.

E. Fletcher Ingals¹ reports the use of adrenalin in a number of rhinological cases. He found that its solution in water sometimes caused smarting, and in one case it was very intense. Acting upon the suggestion of the manufacturers, he thereafter employed normal salt solutions as a solvent, but in such solutions he found that a fungus formed at the bottom within a few days. At the time of his report he was employing the following formula, which had undergone no changes, though it had been in constant use for several weeks:

R.—Adrenalin	gr. j.	gm.	0.065
Acidi borici	gr. lxxx.	gm.	5.000
Aquæ cinnamomi	℥ 1250	c.c.	80.000
Aquæ camphoræ	℥ 1250	c.c.	80.000
Aquæ dest.	q. s.	℥ 2500	c.c.	160.000

From his experiments he was satisfied that a solution of the strength of 1 to 5000, used as a spray, or the powder in the strength of 1 to 5000 or 1 to 2500, with sugar of milk, would be valuable in the treatment of acute inflammatory affections of the nasal passages. In acute coryza or hay fever he believes relief should be obtained by the use of the following formula:

R.—Adrenalin chlorid.	gr. $\frac{1}{16}$	gm.	0.006
Aquæ camphoræ	℥ ss.	c.c.	15.000
Acidi borici	gr. viij.	c.c.	0.5
Aquæ dest.	q. s.	℥ j.	c.c.	30.000

In acute inflammation of the tonsils he believes the strength of 1 to 5000 to be too weak, and that in these cases the solution should be 1 to 1000. In acute and subacute laryngitis, and particularly for the relief of acutely congested cords in vocalists, the application of a 1 to 1000 solution, with moderate force, will so thoroughly reduce the swelling and congestion that the voice may be used for two or three hours with comparative ease and probably with normal effect.

The experiments of Dr. Edward T. Reichert² with adrenalin upon normal and morphinized dogs are extremely interesting. He believes that the toxic effect of morphine or opium is intensified by the profound depression of the general metabolism, which is so wide-spread as to probably involve the processes which are concerned in internal secretion. He experimented with adrenalin on normal and morphinized dogs, and found it was (when administered by the stomach or any other way) a decided circulatory and respiratory stimulant, and that it increased metabolic activity. When administered in such minute doses as 0.00025 per kilogramme weight to normal dogs it had no distinct influence, but in morphinized dogs it prevented the profound decrease of general

¹ Journal of the American Medical Association, April 27, 1901.

² University of Pennsylvania Medical Bulletin, April, 1901.

metabolism and fall of temperature commonly seen after the use of morphine. It is his opinion that in narcosis following the administration of morphine or anæsthetics the secretory processes of the adrenal gland are checked, and that by artificially supplying the active principles of that secretion, respiration, circulation, and general metabolic processes are stimulated. He believes the drug will be found of much value in cases of opium poisoning, in circulatory failure, and to prevent the collapse of anæsthesia. Owing to the powerful vasoconstrictor local action of this substance, abscesses are likely to follow a subcutaneous injection, and it is recommended that, except in urgent cases, it should be administered by the mouth, and mixed with alcohol to increase the rapidity of its absorption.

Tetanus Antitoxin. It is to be regretted that we are still uncertain as to the therapeutic value of this antitoxin. We are convinced by a review of the literature on this subject that the antitoxin in many cases has not been used early enough in the course of the disease or in large enough doses to make it possible to judge of its utility. While we admit that our opinion is not based upon any collective statistics, we are inclined to believe that by the use of Tizzoni's serum better results have been obtained than with some other antitetanic serums. The very best product should be employed, and as it is an entirely harmless substance it should be used in full doses at the earliest possible moment from the beginning of the disease. The experimental studies of L. Zupnik¹ indicate that the location of the infecting wound has an influence on the amount of tetanus toxin elaborated, and therefore on the severity of the disease. He was able to demonstrate that when the tetanus spores or toxins were injected into the dorsum of the foot, the tail or hock of an animal, it caused descending tetanus, similar to that in human beings, and twice as large a dose was required to produce a fatal effect as if injected in the thigh, inguinal region, or any of the large muscles. When injected into the large muscle the toxin constantly induced ascending tetanus.

Dr. W. Wilms² reports four fatalities from tetanus, in all of which cases tetanus antitoxin was used in large doses within thirty hours from the onset of the attack. In all of the cases the condition which Behring requires to be fulfilled was complied with. In none of the patients was there any noticeable improvement. In two cases of chronic tetanus where the serum was not employed until the third day recovery followed. His studies of the statistics of the Leipzig Hospital lead him to believe that the use of tetanus antitoxin was without beneficial

¹ Deutsch. med. Wochenschrift, December 27, 1900.

² Münchener med. Wochenschrift, February 5, 1901.

effect in almost all of the acute cases. He also believes that previous statistics are misleading, as they include many cases of chronic tetanus. Dr. John McCaw¹ reports a case of tetanus neonatorum (in which the diagnosis was confirmed by bacteriological examination) that was successfully treated with antitetanus serum. The infant developed symptoms of trismus on the ninth day after birth, and was first seen by him four days after the first manifestation of the disease. Five cubic centimetres of tetanus antitoxin from the Pasteur Institute were injected (with all antiseptic precautions) under the skin of the abdominal wall. After taking a culture from the foul discharge about it the umbilicus was thoroughly cleansed with boric-acid solution and antiseptically dressed. A teaspoonful of castor oil was administered. As the child was unable to use the nursing-bottle, it was fed by introducing milk in the side of the mouth and permitting it to trickle into the pharynx, the head being held well back. During the entire day the baby's temperature was high, reaching 104° F. It developed severe attacks of spasms each time it was fed or moved. The following day there was some improvement in the spasmodic condition, but the temperature remained high. On the third day of the treatment the infant was able to nurse the bottle, and spasms only occurred when it was fed or moved, but the temperature continued to range quite high, reaching 108° F. at two o'clock in the afternoon. Upon this day 2.5 c.c. of antitoxin were given and ice-bags applied to the spine. The improvement was gradual, but continuous, and the child was discharged from the hospital, cured, about four weeks from the day of its admission. The result of treatment of this disease by tetanus antitoxin has not heretofore been very encouraging. McCaw attributes the successful termination of this case to the early use of large doses of the antitetanic serum to antidote the toxins, and the application of the spinal ice-bag to combat hyperpyrexia. The large number of cases of tetanus reported annually in this country following the celebration of the Fourth of July lead Dr. H. Gideon Wells² and Dr. F. Lewis Taylor³ to insist that, in addition to thoroughly cleansing and draining the wounds received from blank cartridges, the injured should be given a prophylactic dose of 5 or 10 c.c. of tetanus antitoxin.

Tetranitrol, or **Erythrol Tetranitrate**, is said by Huchard⁴ to be one of our most valuable drugs in the treatment of diseased conditions characterized by high arterial tension. Its action is more prolonged than nitroglycerin; it does not alter the hæmoglobin in the blood nor produce the disagreeable pulsating temporals so often seen after the use of

¹ British Medical Journal, March 30, 1901.

² Medical News, June 1, 1901.

³ New York Medical Journal, July 20, 1901.

⁴ Bull. Acad. de Méd., 1901, p. 288.

the nitrites. It is given in doses of from $\frac{1}{4}$ to $\frac{1}{2}$ grain (0.015 to 0.03 gramme) three times a day. When prescribed in the form of pills, powders, or tablets the compounder should not use forcible trituration, as the remedy is explosive on percussion.

R.—Tetranitrol gr. vj. gm. 0.40
Pulvis aromatici gr. vj. gm. 0.40

Misce et ft. chartulæ No. xxiv.

Sig.—One to two tablets two or three times a day.

Thiocol (sulpho-guaiacolate of potassium). This is a fine, white, odorless powder, said to contain 60 per cent. of guaiacol. It is freely soluble in water, has a taste which is not unpleasant, and is not irritating to the mucous membranes. In tubercular affections it is administered in doses of from 1 to 2 grammes (15 to 30 grains) three times a day, and is less liable to disturb digestion than other guaiacol compounds. It may be prescribed in the form of powders, capsules, or cachets, and also in aqueous or hydro-alcoholic solutions. J. A. Goldmann gives the following formula, which he considers suitable for children :

R.—Thiocol 3 ijs. gm. 10.00
Syrupi aurantii q. s. ad 3 iij. c.c. 90.00

Misce. Sig.—One teaspoonful for a child, or one dessertspoonful for adults, three times a day in milk or coffee.

Thyroid Extract. With increasing experience we are coming to understand more clearly the physiological action as well as the therapeutical application of the thyroid extract. When the thyroid gland is removed from the human being he develops mental apathy, diminution of cutaneous sensibility, unsteadiness of gait, lowering of the temperature, dryness of the skin, falling of the hair, a carious condition and loss of the teeth, and a marked increase of mucin in the connective tissue and especially in the skin. There is a decrease of the nitrogenous wastes, and at first there is heightened arterial tension. All of these symptoms are present also (in a modified form) when there is diminished secretion from the gland. When the gland is congenitally absent, in addition to the interference with metabolic changes as recorded above, there is arrest of mental development and bodily growth, a thickening of the cranial bones, stunted growth, particularly of the long bones, with slow ossification of their epiphyses.

When there is hyperthyroidal secretion, or when the extract is administered in excessive amounts, the nervous and mental symptoms are usually marked, being characterized principally by irritability, restlessness, wakefulness, and other symptoms of nervous excitement. The action of the heart becomes extremely rapid—in some cases very irregular—and, while the pulsations are strong, the pulse is of low tension.

Respiration becomes very rapid, and rise of temperature, although not a constant symptom, is usually present. There is loss of bodily weight, increased diuresis, and an increase of phosphates and nitrogenous products.

Among other important functions of the thyroid gland, Cyon¹ believes that it regulates the circulation of and prevents hyperæmia of the brain. Its functional activity is temporarily excited to hypersecretion by emotion, and normally excited to hypersecretion by menstruation and pregnancy. Basing the therapeutic application upon what we know of its physiological action, we would naturally expect it to be of value for the purpose of establishing the proper equilibrium of the central nervous system, as in melancholia and stuporous states, particularly when associated with the disorders of menstruation. It is also used to stimulate the nutrition and for the development of the brain, as in cretinism and myxœdema; to regulate the proper supply of mucin, particularly in the connective tissue, as in scleroderma; to stimulate and assimilate the proper supply of bone salts, as in ununited fracture and in osteomalacia. Through its action upon the blood-supply of the skin, regulating the amount of perspiration and improving the nutrition of the skin, it is of value in the treatment of psoriasis and for excessive sweating. In all of these conditions we have abundant evidence that when applied to the proper cases, with the knowledge of its physiological action and its limitations, it supplies a field in practical medicine for which heretofore we have been without an efficient remedial agent. The value of thyroid extract in myxœdema and cretinism is now so well understood that it is scarcely necessary to more than mention the fact that it represents one of the remarkable achievements of modern therapeutics. In treating cases of this character it is usual to begin with one or two grains of the extract three times a day, and gradually increase the dose until physiological effects are noted. The dose is then slightly reduced, and continued until satisfactory results are secured. After this time it is either given in small daily doses or at regular weekly intervals, to obviate the return of symptoms. As a rule, smaller doses are required during the warm summer months than in cooler weather. The activity of preparations of different manufacturers varies widely, and when using the extract we should be particular to secure the products from a reliable source.

In a discussion before the California Academy of Medicine in November, 1890, Dr. William W. Kerr² called attention to the lack of uniformity in the dose of the extract, and said that the variations in the strength might possibly be due, in some instances, to the source from

¹ *Centralblatt f. Phys.*, Leipzig and Wien, 1897.

² *Journal of the American Medical Association*, January 12, 1901.

which the glands were collected. The glands of American sheep are said to atrophy after they are a year old, and if such is the case the extract should be manufactured from the glands of animals under this age.

Considerable difference of opinion has existed in the past as to the value of thyroid extract in the treatment of cases of insanity. Many writers have testified to its usefulness in some cases and to its harmful effects in others. We believe that if applied to properly selected cases it has a distinct value. The knowledge to be gained from a clinical picture of Graves' thyroid disease, in which there is thyroïdal hypersecretion, with its train of nervous symptoms of cerebral irritability, mental excitement or mania, upon the one hand, and of cretinism and myxœdema—two diseases in which there is hyposecretion accompanied by mental hebetude or stupor—upon the other, apparently clearly indicates the class of cases in which the drug should be used. In certain cases of melancholia, stuporous states, and hypochondria, where a cerebral stimulant is required, thyroid extract should be tried; but in cases of mania and nervous excitement it certainly appears to be contraindicated.

Thymotal (thymol carbolate) is said by J. E. Pool¹ to be made by the influence of phosgen gas on thymolnatrium, and, after purification, is a white, crystalline, insipid substance, with a feeble odor of thymol. In the doses of 30 grains (2 grammes) for adults, 15 grains (1 gramme) for children, and 7.5 grains (0.50 gramme) for infants, three times a day for three days (to be followed on the fourth day by an active purge), he has found it to be of the greatest value in the treatment of anchylostomiasis. He thinks the remedy is preferable to thymol in this disease, because it is without odor and can be more easily taken. It does not break up until it reaches the intestinal tract, and therefore is less liable to be vomited. It does not cause vertigo, as does thymol, and it reduces the danger of thymol poisoning.

Trional. Trional, like sulphonal, is a deservedly popular remedy in the treatment of many cases of insomnia, and, considering its extensive use, there are comparatively few instances in which poisoning has resulted from the drug. That it may produce poisoning of a very serious nature, however, is illustrated by occasional reports of such accidents. When employed for more than a few days at a time its effects should be carefully watched, and, as we have strong evidence that it may produce intoxicating effects by its supposedly accumulative action, measures should be adopted to promote its elimination. These measures consist in keeping the bowels and kidneys active and the administration of citric acid with the drug. Should the urine become dark the remedy

¹ Medical News, March 2, 1901.

must be discontinued at once and the patient encouraged to drink freely of aerated water to which moderate quantities of bicarbonate of soda are added. Stuart Hart¹ reports an interesting case of poisoning in a woman who, during two months, took 15 grains of trional every second day—in all, 400 grains. Her first symptoms were severe abdominal pains of a colicky nature, with nausea and vomiting, and abdominal tenderness and distention. A little later the heart became intermittent, and a systolic murmur developed; also hæmatoporphyrinuria, and after this multiple neuritis, with occasional periods of delirium with hallucinations. There was very great emaciation, and during a prolonged illness her weight fell from 153 to 90 pounds. At the end of the year from the beginning of symptoms the patient was able to walk a little without assistance, and she has since recovered, with the exception of some emaciation and a marked thickening about the joints of the fingers. M. Rosenfeld² reports a case of chronic poisoning and death from trional, in a woman aged twenty-eight years. The drug had been given at irregular intervals for a number of months, and hæmatoporphyrinuria did not occur until the patient had developed marked digestive disturbances, nervous symptoms, and trophic changes. It is his belief that so long as the general nutrition of the patient is good there is little danger of poisoning by trional, but when the bodily weight and general nutrition is lowered there is much more likelihood of its occurring. He apparently verified this belief by experiments upon animals.

Sidonal. This is a white, crystalline compound, made by chemically combining quinic acid with piperazin. It has been employed to a limited extent in the treatment of gout. Its dose is from 5 to 8 grammes (75 to 120 grains) daily. Blumenthal³ experimented with the drug upon healthy men, and found that the uric-acid formation was decreased from 30 to 50 per cent. In the place of uric acid hippuric acid was formed, and the latter, being much more soluble than the former, is rapidly eliminated.

Dr. Saalfeld⁴ reports five cases of gout in which sidonal was employed; pain was relieved, swelling reduced, and the nodules diminished in size, and in some other cases the gouty nodules entirely disappeared. The drug was found to be ineffective in a case of acute articular rheumatism. The following will be found a convenient form of prescribing:

R.—Sidonal 3j. gm. 30.00

Pone in cachetas No xxx.

Sig.—One to three cachets three times a day.

¹ American Journal of the Medical Sciences, April, 1901.

² Berliner klin. Wochenschrift, May 20, 1901.

³ Ibid., 1900, p. 332.

⁴ Münchener med. Wochenschrift, April 10, 1901.

Urea. This substance has been employed to a limited extent as a diuretic and also as a uric-acid solvent. If the favorable reports of Dr. Henry Harper¹ are confirmed by others we will be in the possession of a remedy whose value in the treatment of tuberculosis is beyond estimation. Harper does not underrate the beneficial influences of pure air, food containing a superabundance of urea, cod-liver oil, creosote, guaiacol, arsenic, iron, hydrochloric acid, pepsin, strychnine, etc., but, in conjunction with these, he considers urea to be a remedy superior in value to any other used at the present time in the treatment of tuberculosis. He maintains that when administered to tubercular subjects urea is a constructor and builder of tissues, and that "pure air and rich food containing a superabundance of urea render the tissues and fluids of the body proof against the bacilli finding a suitable soil; in short, they act as an antitoxin." He also believes that persons afflicted with gout and allied diseases are to a great extent immune to tuberculosis. In two recent reports he gives the record of fourteen cases of tuberculosis (all confirmed by microscopical examination), some of which were very advanced cases, in which cures or decided amelioration of the symptoms were effected by his method of treatment. In these cases urea was usually administered by the mouth in doses of about 20 grains (1.30 grammes) three times a day, though in some of the cases (the drug being very soluble in water) it was given hypodermically.

A. H. Buck² employed urea with satisfactory results in the treatment of a severe case of lupus involving the face, nose, and mucous membranes of the mouth and nasal cavity. Two weeks after beginning the remedy the edges of the ulcers became more healthy in appearance, and healed rapidly, so that in a short time all of the ulcers were healed. In this case urea was administered at first in doses of 30 grains (2 grammes) three times a day, and increased later to 1 drachm (4 grammes) at each dose. The disease had failed to yield to any other form of treatment, and gradually grew worse during the past year, and as no other changes were made in the habits or treatment of the patient the good results were attributed entirely to the use of urea.

R.—Urea ʒj. gm. 30.00

Ft. chart. No. xxiv.

Sig.—One powder dissolved in cold water, three times a day.

Urosin. Urosin is a crystalline substance said to be made from a lithian salt of chinic acid. In doses of 7 to 10 grains (0.50 to 0.6 gramme) three times a day it has been employed with asserted success in the treatment of acute gout.

¹ *Lancet*, March 9 and June 15, 1901.

² *Practitioner*, July, 1901.

R.—Urosin 3iv. gm. 16.00
 Pone in cachetas No. xxiv.
 Sig.—One to two cachets three times a day.

Urotropin. Ammonium Formamide. The reports bearing on the value of urotropin as a urinary antiseptic are uniformly favorable, but as a solvent for renal and cystic calculi (for which it was originally suggested by Nicolaier) it has been shown to be useless. The statement of Casper, that urotropin, in the presence of acids, is decomposed, with the formation of formaldehyde, has been generally accepted, but recently P. I. Cammidge¹ has proven that this change occurs only when solutions of the drug are heated, and does not take place within the body. He demonstrated that the urine of persons taking as much as 30 grains of urotropin a day did not contain formaldehyde, and he thinks it probable that the antiseptic properties of the drug are due to the formation of new urotropin compounds. He also determined that the drug was not a diuretic.

It is known that the urine of persons convalescent from enteric fever frequently contains typhoid bacilli for from two to four weeks after they are up and around, and it has been demonstrated clinically that the urine of typhoid patients may be cleared of the bacilli by the administration of urotropin; therefore, it has become customary with many physicians to administer the drug during and after such attacks, so as to lessen the danger of infection to others. That this plan is not free from harmful effects has been shown by W. Langdon Brown,² who reports two cases in which hæmaturia followed the daily administration of urotropin. In both instances the patients were suffering with enteric fever, and urotropin was being given in doses of 10 grains (0.6 gramme) three times a day. The hemorrhage occurred in both upon the eighth day of urotropin medication, and was thought to have originated in the bladder. Dr. Brown thinks that the discomfort which precedes the hæmaturia should be a danger signal when the drug is employed in such cases.

Veratrum Viride. The weight of evidence is to the effect that, when administered fearlessly but intelligently in properly selected cases, veratrum viride is a remedy of considerable value for preventing and controlling puerperal convulsions. The remedy is not indicated in all cases of eclampsia, and is intended to be applied in conjunction with other judicious remedies in treating cases of this character. When the pulse is full, strong, and of high tension the drug is indicated, but it is considered both useless and dangerous if the heart is weak and the

¹ *Lancet*, January 15, 1901.

² *British Medical Journal*, June 15, 1901.

pulse feeble and compressible. Having once decided to give it to prevent or control eclamptic seizures, veratrum viride should be administered boldly and for effect. From 20 to 40 minims of the tincture, or from 10 to 15 minims of the fluid extract, should be given hypodermically as an initial dose, and repeated in somewhat smaller quantities every fifteen to thirty minutes until the convulsions are controlled or until the pulse becomes compressible and its rate lowered to about 60 beats per minute. It is claimed upon good authority (Jewett, Parvin, Hirst) that convulsions seldom or probably never begin nor recur if the pulse-rate is kept below 60. Although we have learned to know in what class of cases to use the drug, we do not yet understand how it does good. Among the different hypotheses advanced to explain the beneficial action of veratrum viride in eclampsia are the following: It depresses the motor side of the spinal cord, thereby preventing the transmission of impulses from the centre to the periphery; its powerful vasomotor influence prevents the determination of too great a quantity of toxin-laden blood to the brain; its stimulating effect upon the sweat-glands, salivary glands, and excretory cells of the liver eliminates and destroys the toxins. (Isham.) It causes retraction of the neurones, thereby cutting off the irritation from centres to periphery and from periphery to the centres. (Isham.) It must be admitted that none of these hypotheses has been accepted as satisfactory. The most valuable recent communications relating to the value of veratrum viride in the treatment of eclampsia appear in the *Therapeutic Gazette* of August 15, 1901. The editor of that journal addressed letters to some of the most prominent obstetricians, asking them to briefly express their views upon the utility of veratrum viride in eclampsia. In response to this letter Dr. J. Clifton Edgar, Professor of Obstetrics in the Cornell University Medical School, stated that for the immediate control of convulsions veratrum viride stands second only to chloroform in efficiency. It relaxes the rigidity of the cervical ring and causes prompt diaphoresis and diuresis. As an initial dose he usually gives from 10 to 20 minims of the fluid extract, or half that quantity of Norwood's tincture subcutaneously, and repeats every twenty or thirty minutes until the pulse continues below 60. He never uses the drug except when the pulse is strong and rapid, and considers it invaluable when temporizing means must be resorted to until we can secure dilatation of the cervix and empty the uterus under deep anæsthesia.

Dr. Richard C. Norris, physician in charge of the Preston Retreat, Philadelphia, replied that in suitable cases he had come to regard veratrum viride as second only to free purgation, and that by judiciously employing the remedy he has seen the nervous symptoms disappear and convulsions apparently warded off. In cases of eclampsia with full,

quick pulse he administers hypodermically 8 minims of the fluid extract of *veratrum viride*, and within fifteen minutes (if necessary) gives another dose of 5 minims. After that time, watching the pulse from hour to hour, the fluid extract is repeated, in doses of 5 minims, sufficiently often to keep the pulse down to 70 or 80. He has usually found it necessary to administer from 30 to 60 minims throughout twenty-four hours. His personal experience leads him to believe that it is not a safe plan to give such large doses as 20 drops of the fluid extract, but thinks the best results are obtained, with the least possible danger, by using smaller doses at frequent intervals. Dr. Barton Cooke Hirst, Professor of Obstetrics in the University of Pennsylvania, stated that after an experience of twelve or thirteen years with *veratrum viride* in eclampsia, he had great confidence in its efficacy. He uses the drug only in cases with a strong, bounding pulse, with suffused face and danger of cerebral apoplexy. Usually he gives 15 or 20 drops of the fluid extract hypodermically as an initial dose, and repeats it in 5-drop doses if the pulse rises rapidly. He has once or twice seen poisoning result from its use, but it was not serious, and was easily manageable by stimulants. Dr. Edward P. Davis, Professor of Obstetrics in the Jefferson Medical College of Philadelphia, answered that in cases of eclampsia with full, heavy pulse and increased arterial tension, the drug diminishes the tendency to convulsions and promotes dilatation of the cervix. He favors the hypodermic administration of the tincture in doses of 10 drops, repeated every hour until the tension of the pulse is decidedly reduced and its rate falls to below 90. Dr. G. M. Boyd, Professor of Obstetrics in the Medico-Chirurgical College of Philadelphia, had employed the drug, but believes it of doubtful value. Dr. Reynolds Wilson, Obstetrician in charge of the Lying-in Charity, Philadelphia, places no dependence upon *veratrum viride*. Dr. Whitridge Williams, Professor of Obstetrics in the Johns Hopkins University, Baltimore, stated that he had no experience with the remedy, and had never been able, from reports of others, to convince himself of its value. Dr. Edward Reynolds states that he has had no experience with *veratrum viride*, but believes that a drug so long employed in the treatment of eclampsia could not have failed of universal adoption if the claims of its advocates were true. In a recent paper by Dr. T. J. Beattie, of Kansas City,¹ he expresses the belief that *veratrum viride* is more extensively employed and highly recommended at the present time than any other single drug used in eclampsia. In the discussion which followed the reading of this paper, Drs. E. C. Bonifield, of Cincinnati, A. B. Cates, of Minneapolis, and B. F. Crummer, of Omaha, agreed that

¹ Journal of the American Medical Association, August 24, 1901.

veratrum viride is a remedy of undoubted value in many cases of eclampsia. Dr. A. B. Isham¹ employs veratrum viride not only in treating puerperal convulsions, but as an eliminant in other forms of toxæmia. It is taken for granted that the reader fully understands that veratrum viride is not the only drug employed by its advocates in the treatment of eclampsia, but in selected cases is administered in conjunction with other drugs and measures of recognized value.

¹ Medical News, March 2, 1900.

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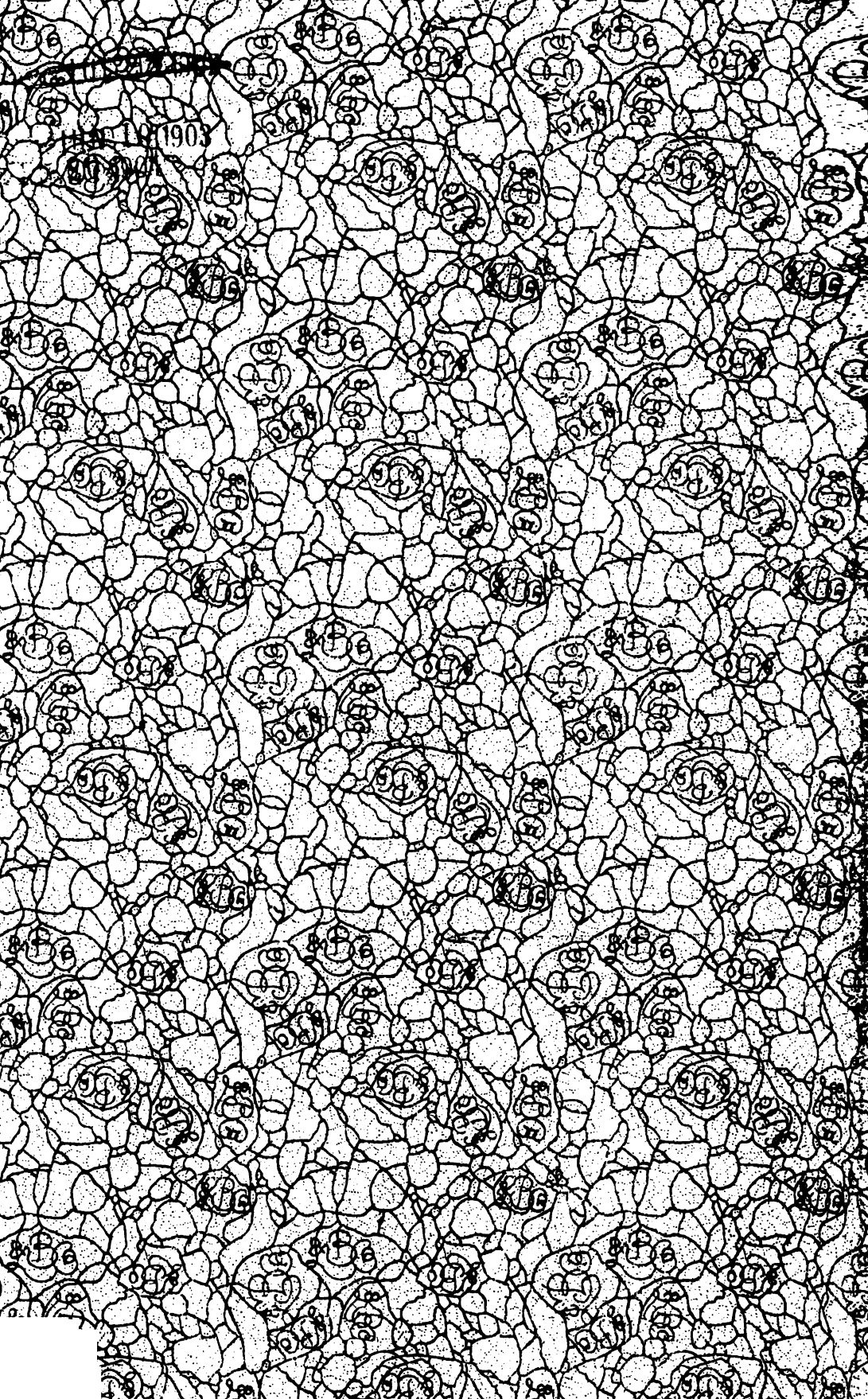
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